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OF
THE JOHNS HOPKINS HOSPITAL

(THE PUBLICATION OF THE MEDICAL SCHOOL AND HOSPITAL)

(SUPPORTED BY THE DE LAMAR FUND OF THE JOHNS HOPKINS UNIVERSITY)

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Medical
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MORTALITY IN TUBERCULIN-POSITIVE INFANTS[1]

MIRIAM BRAILEY, M.D., Dr.P.H.

From the Department of Epidemiology[2] of the Johns Hopkins University School of Hygiene and Public Health, and the Department of Pediatrics of the Johns Hopkins Hospital

Submitted for publication June 6, 1936

The material for this note is derived from the experience of the special out-patient clinic for childhood tuberculosis which has been in operation under the direction of Dr. E. A. Park at the Harriet Lane Home of the Johns Hopkins Hospital since 1928. Admissions to the special clinic are limited to infants who, before two years of age, are shown to be either infected with tuberculosis as demonstrated by a positive tuberculin test, or who are in imminent risk of infection because of familial contact with sputum-positive tuberculosis. After the patient has been registered in the clinic, supervision and study are continued as long as possible, but as the clinic was established only in 1928, not many of these patients have been under observation more than five years.

This study deals with the record, up to November 1, 1934, of the patients registered in the clinic during the five-year period from November 1, 1928, to November 1, 1933. From the total registration of 358 have been selected all those who had a positive tuberculin test prior to two years of age, an x-ray of the chest taken at the time of the test, and had remained under observation at least one year subsequent to this test unless dying sooner. The third condition excluded five patients otherwise eligible, four of the families having refused coöperation and the other having removed from the city after seven months. Patients fulfilling all three conditions totaled 170,[3] of whom 72 were white and 98 were colored.

[1] Aided by grants from the Milbank Memorial Fund, the Commonwealth Fund, and the Maryland Tuberculosis Association.

[2] Grateful acknowledgment is made of the assistance of Dr. W. H. Frost, Professor of Epidemiology, who directed the compilation and analysis of data from clinical records.

[3] Twelve of these children were already known to the Harriet Lane as infected

On November 1, 1934, when these records were compiled, all of the 170 children in the group had been on the clinic register as tuber-

TABLE I

Total observed life experience and mortality following first x-ray in 170 children infected with tuberculosis before two years of age

TIME-PERIOD IN MONTHS AFTER FIRST X-RAY	NUMBER UNDER OBSERVATION AT THE BEGINNING OF THE TIME-PERIOD	NUMBER WITHDRAWN ALIVE FROM OBSERVATION DURING PERIOD*	NUMBER DYING DURING TIME-PERIOD	AVERAGE NUMBER UNDER OBSERVATION FOR COMPUTING MORTALITY	PERCENTAGE DYING DURING THE TIME-PERIOD	PERCENTAGE SURVIVING DURING THE TIME-PERIOD	PERCENTAGE SURVIVING THROUGH PRECEDING AND CURRENT TIME-PERIODS	PERCENTAGE DYING DURING PRECEDING AND CURRENT TIME-PERIODS
x	l_x	w_x	d_x	$l_x - \frac{w_x}{2}$	$100q_x$	$100p_x$	$100P_x$	$100(1 - P_x)$
White								
0–6	72	0	5	72.0	6.9	93.1	93.1	6.9
6–12	67	0	2	67.0	3.0	97.0	90.3	9.7
0–12	72	0	7	72.0	9.7	90.3	90.3	9.7
12–24	65	16	0	57.0	—	100.0	90.3	9.7
24–36	49	12	0	43.0	—	100.0	90.3	9.7
36–48	37	6	0	34.0	—	100.0	90.3	9.7
48–60	31	9	1	26.5	3.8	96.2	86.9	13.1
Colored								
0–6	98	0	14	98.0	14.3	85.7	85.7	14.3
6–12	84	0	7	84.0	8.3	91.7	78.6	21.4
0–12	98	0	21	98.0	21.4	78.6	78.6	21.4
12–24	77	24	2	65.0	3.1	96.9	76.2	23.8
24–36	51	16	2	43.0	4.6	95.4	72.6	27.4
36–48	33	5	0	30.5	—	100.0	72.6	27.4
48–60	28	16	1	20.0	5.0	95.0	69.0	31.0

* Period of observation less than five years because of registration in clinic subsequent to November 1, 1929.

infants prior to November 1, 1928, when they were transferred to the clinic. Three of the twelve, although less than two years of age when found to be infected, were more than two years old when the special clinic opened. On November 1, 1928, their ages were respectively 24 months, 29 months, and 44 months. For these twelve patients observation has been dated from the discovery of infection rather than from the date of registration in the special clinic.

culin-positive for at least one year; hence the rate of mortality during the first year following the discovery of infection may be expressed very simply by stating the number of deaths within the first year as a percentage of the whole number registered (Table I). To express accurately the rate of mortality for a longer period—say five years—it is necessary to take into account the fact that the numbers available for calculation are necessarily diminished as time is extended, since many of the children included came into the clinic considerably less than five years prior to November 1, 1934. Therefore, the computation must be made step by step, following conventional actuarial procedures as shown in Table I. Obviously the numbers under observation are much too small to yield stable rates

TABLE II

Mortality during various periods after discovery of infection in 72 white and 98 colored children found to be tuberculin-positive before 2 years of age

INTERVAL IN MONTHS FROM DISCOVERY OF POSITIVE TUBERCULIN	NUMBER OF DEATHS		MORTALITY PER CENT DURING INTERVAL	
	White	Colored	White	Colored
0–6	5	14	6.9	14.3
6–12	2	7	3.0	8.3
0–12	7	21	9.7	21.4
12–60	1	5	3.4	9.6
0–60	8	26	13.1	31.0

of mortality in each single year. However, the rates indicated for the first year under observation and for the whole five-year period have a fairly definite significance.

Table II shows in summary, as derived from Table I, the mortality for white and colored children separately, in the first six months; the second six months; the entire first year; the next four years; and for the five-year period following the discovery of infection. It should be borne in mind that all children of the series were less than two years old when found to be tuberculin-positive, the average age for each race at the time of the first[4] positive tuberculin test being thirteen months.

[4] Very rarely could the time of infection be more accurately dated by preceding negative tests.

In both races the mortality within the first six months after the discovery of infection is approximately twice as great as in the second six months; and within the first year as a whole it is approximately two and one-half times greater than in the whole of the next four years. About 70 per cent of the mortality for the entire five-year period occurs during the first year of observation.

TABLE III

Mortality in 170 tuberculin-positive infants during (1) the first year, and (2) the five years following discovery of infection: according to lesion shown at initial x-ray

FINDINGS ON FIRST EXAMINATION	RACE	NUMBER OF CASES	DEATHS			
			Within 1 year		Within 5 years	
			Number	Per cent	Number	Per cent
A. Parenchymal lesion	W	23	7	30.4	8*	38.6
	C	44	14	31.8	16*	40.5
	Total	67	21	31.3	24**	40.0
B. Bulging tracheobronchial nodes	W	18	0	—	0	—
	C	18	2	11.1	4*	25.3
	Total	36	2	5.6	4*	12.7
C. Negative chest x-rays	W	31	0	—	0	—
	C	36	5**	13.9	6**	17.3
	Total	67	5**	7.5	6**	9.2
B and C combined	W	49	0	—	0	—
	C	54	7**	13.0	10***	21.3
	Total	103	7**	6.8	10***	11.1

* Indicates 1 death from non-tuberculous cause, there being a total of 5 in five years.

With reference to Table II, it is to be noted that, at every time interval shown, the colored children suffered a mortality more than twice that suffered by white children. Within the first year of observation the mortality was about 10 per cent in white children and 21 per cent in colored children, and for the whole five-year period it was 13 per cent for white and 31 per cent for colored children. Stated conversely, these observations indicate that the chance of survival through five years subsequent to infection discovered before two years of age was 87 per cent for the white and 69 per cent for colored children.

When the 170 patients are classified according to x-ray findings at the first examination, 67 of them showed definite lesions in the parenchyma of the lung, usually accompanied by enlarged tracheo-bronchial nodes. About one-third of these (22) were actually ill when first seen and presented fairly conclusive evidence of pulmonary tuberculosis apart from x-ray findings. In the remaining 45 who were brought for observation and not because of illness, ordinary physical examination was negative, and the diagnosis could not have been made without the use of tuberculin and x-rays.

There were 103 children whose initial x-rays showed no definite involvement of the lung parenchyma. Of these, 36 showed enlargement of the mediastinal shadow with definite bulging of the tracheobronchial nodes; while 67 showed no definitely abnormal shadows at first x-ray, and were therefore designated as roentgenologically negative on admission.

The mortality in these three classes of patients during the first year of observation and during the whole five-year period is shown in Table III. In group A of the table, of 67 children showing unquestioned pulmonary involvement when first x-rayed, 21 were dead within the first year, a rate of 31 per cent, while 3 additional deaths (2 of which were not attributable to tuberculosis) occurred during the next four years, raising the five-year rate to 40 per cent. It is to be noted that the rates for white and colored, once parenchymal lesion was found to be present, were practically identical.

If we select from group A the 22 patients who were ill with tuberculosis when first examined and whose lesions were sufficiently far-advanced to produce physical signs, the extremely high first-year mortality of 68 per cent was found; and this rose to 82 per cent for the entire five-year period. The mortality for such extensive disease was the same for children of both races.

Of the 24 deaths which occurred during the five-year period of observation in group A of Table III, 22 were due to tuberculosis. The immediate cause of death in 11 of the 22 was tuberculous meningitis, while generalized tuberculosis brought about death in 6 others. The five remaining patients were thought to have merely extensive pulmonary lesions, but in three of these upon whom a postmortem examination was performed, an unsuspected miliary tuberculosis was

found to be present. It is clear that extrapulmonary involvement was reponsible for at least 75 per cent of the tuberculous deaths.

Referring to children of group B and C as shown in Table III, there were 103 of these patients who displayed no parenchymal lesion at initial x-ray; they were either x-ray-negative when first seen, or they showed only enlarged tracheo-bronchial nodes on first examination. Their combined mortality for the first year of observation was 6.8 per cent, and for all five years 11.1 per cent. These rates are roughly one-fourth those for children coming under observation with parenchymal lesion and followed during the same time-periods.

The observations show no significant difference in total mortality between children admitted with bulging nodes (B) and those admitted as x-ray-negative (C).

TABLE IV

Classification of initial chest findings in 170 tuberculin-positive infants, white and colored

FINDINGS ON FIRST EXAMINATION	WHITE		COLORED	
	Number of cases	Per cent	Number of cases	Per cent
Parenchymal lesion	23	31.9	44	44.9
No parenchymal lesion	49	68.1	54	55.1
Total	72	100.0	98	100.0

However, mortality in the two races in children admitted without parenchymal lesion is significantly different. Among 54 colored children 7 deaths occurred during the first year of observation, a rate of 13 per cent. This rate increased to 21 per cent by the end of five years of observation. During the same five-year period of time, no deaths occurred among 49 white children.

Of the 10 deaths occurring among these 54 colored children during the five years of observation, 7 were attributable to tuberculosis, 5 falling in the first year of observation and 2 somewhat later. One child died of miliary tuberculosis without meningitis. Tuberculous meningitis was the immediate cause of death in the remaining six. In two of the six the meningeal involvement was preceded by miliary tuberculosis. The remaining four of the six meningeal patients were

thought, during life, to have no parenchymal lesion, but in three who underwent postmortem examination, well-defined pulmonary lesions were discovered. All the deaths due to tuberculosis in children admitted without parenchymal lesion were due to extra-pulmonary involvement.

TABLE V

Rate of development of parenchymal involvement during (1) the first year and (2) the five years subsequent to discovery of infection in 102 infants showing no parenchymal involvement at first x-ray, white and colored

RACE	NUMBER OF CASES	PARENCHYMAL LESIONS			
		Within 1st year		Within 5 years	
		Number	Per cent	Number	Per cent
White	48	1	2.1	2	5.8
Colored	54	12	24.0	13	28.0
Total	102	13	13.4	15	17.2

TABLE VI

Mortality during first year and during five years of observation in 170 tuberculin-positive infants, according to age when infection was discovered

AGE IN MONTHS AT DISCOVERY OF INFECTION	NUMBER OF CASES	DEATHS			
		Within 1 year		Within 5 years	
		Number	Per cent	Number	Per cent
0–6	21	7	33.3	11	77.6
6–12	45	7	15.6	8	18.0
12–24	104	14	13.5	15	15.1
0–24	170	28	16.5	34	23.2

The higher mortality observed in the colored children of this series appears to be attributable to their greater tendency to develop parenchymal lesion. This is shown partially by the results of the initial x-ray examination, at which 45 per cent of the colored and 32 per cent of the white infants showed pulmonary involvement. It is still further shown by the greater frequency in colored children of subsequent development of parenchymal lesions in those who showed none when first admitted, as is seen in Table V.

In this table are included only those children who, on first examination, showed no parenchymal lesion and for whom there was at least one subsequent x-ray. For the first year subsequent to admission parenchymal lesions developed at the rate of 2.1 per cent in the white and 24 per cent in the colored children. For the five-year period subsequent to admission, as nearly as can be estimated from the scant data available, the indicated proportions developing parenchymal lesions are 5.8 per cent in white and 28 per cent in colored infants.

It is thus evident that in this series colored children infected with tuberculosis developed parenchymal lesion much more frequently than did the white, but once such lesion had developed, the risk of death was not materially different in the two races.

Clinical experience would appear to indicate that mortality is related to age at which infection develops, the prognosis being more unfavorable the younger the child. That this is so in our series is shown in Table VI, where the patients are grouped according to the age at which the tuberculin test was found to be positive. The proportions of white and colored, respectively, are substantially identical in the three age-groups shown in this table and in consequence no separation is made for race. Children found to be infected before six months of age had a mortality of 33.3 per cent within the first year of observation, and of nearly 78 per cent within five years subsequent to the discovery of infection. Both the first-year and five-year rates drop sharply for children whose infection was demonstrated after six months of age, the rates being much alike for infections discovered during the second six months of life or during the second year of life. Combining the two latter age-groups, the first-year mortality was 14 per cent and the five-year mortality was about 16 per cent. These rates vary significantly from those for infants *known* to have been infected before six months of age.

It is quite reasonable to suppose that the mortality in this whole series has been higher than the average for children infected within the same age limit; because the children in this study come from the poorer strata of the population and a large proportion of them had been in intimate and more or less prolonged household contact with open cases of pulmonary tuberculosis. Such contact was definitely established in 78 per cent of the white and 64 per cent of the colored

children. In the remainder of the cases careful investigation revealed no intra-familial source of infection; but, as it was not possible to make a complete examination of every member of every family, it is possible that there may have been undiscovered cases of tuberculosis in some of the families which gave negative histories.

Since it is generally believed that the severity of infection with the tubercle bacillus is directly related to the size of the infective dose or to the frequency and duration of repeated infection, the records of these children have been carefully studied to ascertain whether or not they show such a relationship; that is, whether the children exposed to demonstrable intra-familial sources of infection tended to suffer a higher mortality than those for whom no such exposure could be found. The questions involved are more complex than at first appears and can be discussed fully only in a more detailed presentation than can be given at this time. For the present it can only be said that no obvious relationship of this kind has been shown. White children of this series in contact with a sputum-positive case showed a mortality of 14.8 per cent for the first five years, while those not known to have had such contact within the family suffered a mortality of 6 per cent in the same period. Colored children in known familial exposure had a five-year mortality of 33.9 per cent, as against 25 per cent in those with negative contact history. However, while these differences are suggestive they are not definitely significant in such a small series; and further study of a larger series of cases is required for definitive information.

SUMMARY

1. One hundred seventy children, of whom 72 were white and 98 colored, found to be infected with tuberculosis before reaching two years of age, have been kept under observation for periods ranging from one to five years.

2. They can be divided into 67 who showed parenchymal involvement of the lungs at initial x-ray and 103 who showed no definite parenchymal lesion when first examined. Twenty-two, roughly one-third of those with pulmonary lesion when infection was discovered, were ill and presented signs of disease such that a diagnosis could usually have been made by ordinary clinical means. The remaining

patients gave no indication of their infection, and a diagnosis could not have been made without the tuberculin reaction and the use of the x-ray.

3. By calculation, following actuarial procedures, the total five-year mortality for white children was found to be 13 per cent and for the colored 31 per cent.

4. Approximately 70 per cent of the deaths which occurred in five years of observation fell within the first year, mostly within the first six months following the discovery of infection. This refers to deaths from all causes, but, with very few exceptions, tuberculosis was the immediate cause of death.

5. Of those admitted with involvement of the lung parenchyma, 31 per cent were dead within the first year of observation, no difference being observed between the two races in case fatality.

6. Among those whose initial chest plates showed no parenchymal involvement, mortality during the first year subsequent to the discovery of infection was 6.8 per cent. No deaths occurred among the 49 white children of this group, but there were 7 deaths among 54 colored children.

7. In the entire group of colored children observed, mortality has been more than twice that observed in white children.

8. When the pulmonary lesion has developed sufficiently to be readily demonstrable by x-ray, the fatality is about the same in white as in colored children. However, lesions of this extent are very much more frequent in the colored than in the white, and this appears to account for the fact that the gross mortality in the colored is so much higher.

9. In both white and colored children, mortality has been more than twice as high in those known to be infected during the first six months of life, as in those whose infection was discovered between the ages of six months and two years.

10. In about 78 per cent of the white and 64 per cent of the colored children of this study there was intra-familial contact with a proved sputum-positive case. The children of each race with known exposure showed a slightly higher mortality than children not known to have been exposed. The difference in mortality is not statistically significant and a detailed study of a larger series must be made to determine the bearing which continued exposure may have upon severity of lesion.

THE INFLUENCE OF THE ADRENAL CORTEX UPON THE DISTRIBUTION OF BODY WATER

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Submitted for publication June 8, 1936

One of the most constant features associated with the withdrawal of injections of adrenal cortical hormone from the bilaterally adrenalectomized dog is concentration of the blood.[1] This is manifested by a rise in erythrocyte count and hemoglobin, an increased proportion of packed red cells to plasma in hematocrit determinations and an augmented concentration of the plasma proteins (1). A loss of fluid evidently takes place from the circulating blood, and Swingle and his coworkers (2), as well as Hetzel (3), have shown clearly the contraction in circulating blood volume which occurs under these circumstances.

A moderate diuresis frequently accompanies the increased urinary excretion of sodium, following adrenalectomy, as originally shown by Loeb (4). It also follows extract withdrawal from the adrenalectomized animal (5), and might be assumed to be the chief factor responsible for the blood concentration. This excretion, however, as Swingle and others have pointed out (6), is not sufficient to account for the apparent loss of fluid, particularly if it be assumed that a similar contraction in volume occurs in all of the other extracellular fluids as well as the plasma. It is in fact possible, as we have recently shown (7), by forcing fluids upon the adrenalectomized dog during the progress of

[1] The methods employed in this laboratory for the preparation and care of adrenalectomized male dogs, which we have used exclusively, have been previously described (1, 5). All blood and plasma determinations have been done on blood drawn from the femoral artery and prevented from clotting with purified heparin, as previously detailed. Hematocrit determinations were made by centrifuging the blood at high speed for 20 minutes in Wintrobe tubes. The red blood cell counts and hemoglobin estimations were all performed by Miss Regina Weistock. Plasma proteins were estimated by the macro-Kjeldahl method.

insufficiency, after withdrawal of extract injections, to avoid any appreciable disturbance of water balance at all or significant loss of weight, although the hemoconcentration and the toxic phenomena characteristic of cortical insufficiency progress as usual.

If the contraction of the blood volume is actually due to a loss of fluid from the plasma, and no other alternative seems possible, it could be ascribed either to drainage from the blood capillaries, which allows fluid to pass into the interstitial tissue spaces, or it may be postulated that an actual withdrawal of fluid, from the blood plasma and from the interstitial spaces as well, takes place into the tissue cells.

The first view was proposed by Swingle, who considers that the signs and symptoms of adrenal insufficiency are practically identical with those of traumatic or of secondary shock (8), although recently he has shown that no fall in plasma sodium attends the production of traumatic shock in the intact animal (9). He believes that the hormone influences the normal exchange of water and salts between blood vessels and tissues, and acts as a regulator of the blood volume. In the absence of the hormone "the blood water slowly transudes into the tissues and interstitial tissue spaces and is immobilized." The same general idea had been expressed earlier by many others, including Wyman (10), who compared the effect of adrenal insufficiency in the rat to that of anaphylactic shock, or of histamine poisoning, and believed it to be due to "inability to maintain capillary tone and normal permeability." Gradinescu (11), Winter and Hartman (12), Viale and Bruno (13), and Britton and Silvette (14), have expressed somewhat similar views. A common conclusion among observers has been that in the absence of the adrenal cortical hormone some disturbance of normal capillary exchange occurs, and there is an escape of fluid from the vessels into the surrounding tissues.

The second view, namely, that a withdrawal of fluid occurs from both plasma and interstitial spaces actually into the tissue cells as a result of the unbalanced isotonic equilibrium caused by the renal excretion of sodium, has been proposed by Darrow and Yannet (15) and by Gilman (16), who have based their conclusions upon the analogy to experiments upon intact animals given injections of intraperitoneal glucose. The experimental work detailed in the present communication appears in part to support this second theory.

TABLE 1

Dog 160. The effect of the injection of cortical extract alone upon the fluid and electrolyte balance of the animal in insufficiency

The diet was constant (standard dog ration) from September 22. On the morning of October 3 (the seventh day after withdrawal of extract) the animal was severely intoxicated. Fifty cubic centimeters of extract were given in divided doses, neither additional water nor food being given. This produced dilution of the blood and excretion of 305 cc. urine with retention of sodium. The loss of potassium was several-fold greater than could be accounted for by the reduction in its concentration in the extracellular fluids, should the fall have been commensurate with that observed in the plasma.

DATE	WEIGHT	FOOD	EXTRACT PER DAY	WATER INTAKE	URINE OUTPUT	SODIUM OUTPUT	POTASSIUM OUTPUT	NITROGEN OUTPUT	PHOSPHATE OUTPUT	PLASMA SODIUM	PLASMA POTASSIUM	NPN	ERYTHROCYTES	PLASMA PROTEINS	VOLUME PACKED RBC (HEMATOCRIT)
1935	*kgs.*	*gms./day*	*cc.*	*cc.*	*cc.*	*m.eq.*	*m.eq.*	*gms.*	*mgs.*	*m.eq./l.*	*m.eq./l.*	*mgs.%*	*millions per cu.m.*	*gms.%*	%
Sept. 23	7.3	450	4									31			
Sept. 28	7.1	450	0									44			
Sept. 30	7.0	410	0									55			
Oct. 2–3	7.0	200	0	None	159	+2.4	−0.1	+0.3	127			58			
										131.3	12.0	104	6.0	8.7	51
Oct. 3–4	6.8	None	50	None	305	+1.3	−36.6	−6.4	531						
										136.4	6.6	54	5.2	7.5	35
Oct. 4–5	6.5	450	30	345	232	+8.4	+3.1	−1.7	371						
										136.3	6.1	42	4.8	7.3	36

EXPERIMENTAL

A. The influence of the cortical hormone upon the distribution of water and electrolytes in the adrenalectomized animal in adrenal insufficiency, even when all exogenous fluids and salts are withheld, is indicated in the following experiment (Table 1).[2]

An adrenalectomized dog previously sustained in good condition with injections of cortical hormone, was deprived of extract, which gradually precipitated the usual toxic symptoms. On the seventh day (October 2–3) all fluid was withheld. During the following twenty-four hours, food as well as fluids was withheld, but 50 cc. of cortical hormone in divided doses were injected subcutaneously. Prompt clinical improvement during the next twenty-four hours was associated with a marked diuresis (305 cc.), in which the urinary excretion of potassium and of phosphate was increased about four-fold, and the excretion of nitrogen almost trebled. A sharp drop in body weight took place (6.8 to 6.5 kgs.). At the same time, in spite of the diuresis, and in the face of complete withdrawal of food and fluid, the blood became diluted. A marked fall also occurred in the concentration of plasma non-protein nitrogen and potassium. The injection of an effective amount of the hormone, therefore, in the adrenalectomized dog receiving neither food nor water, brought about both dilution of the blood plasma and appreciable diuresis. At the same time an excretion of potassium, phosphate and nitrogen took place which was so considerable in quantity that it must have been derived not only from the amounts present in the interstitial fluids but from the tissue cells as well.

B. Further information regarding the movement of body fluids during withdrawal and reinjection of the cortical hormone may be derived from direct measurements of the interstitial fluid volume by methods recently devised. Of these, Lavietes (17) has produced evidence that the most suitable is that employing sodium thiocyanate. The method of Crandall and Anderson (18) using sodium thiocyanate for determination of the volume of extracellular fluids of the body, has been subjected recently to further critical study by Lavietes, Bourdillon and Klinghoffer (19), who have compared in man the

[2] Similar experiments have been published by Swingle and his co-workers (6) but without detailed chemical studies.

results obtained with this substance, with those obtained with sucrose and sodium sulphate. The method involves the injection of a diffusible, non-toxic and non-metabolized material, not normally present in the body, which diffuses rapidly and equally over the body fluids, but which does not enter the tissue cells. They concluded that all three of these substances are distributed through approximately the same fraction of the body fluids in man. Of the substances studied, SCN has the advantages of more rapid distribution, slower excretion, and greater ease of estimation. However, it is said to enter the erythrocytes, and in part to be bound in the serum. They estimated the concentration of SCN in transudates as 10/11 of that of the serum.

Crandall and Anderson studied the rate of excretion in dogs and found that little variation in the serum concentration occurred during the three hours following its injection. They found by this method that the fluid in dogs represented on an average 32.5 per cent of the body weight, the maximum being 36 per cent and the minimum 27 per cent in 33 animals, a value distinctly and perhaps erroneously higher than that found in man, which Lavietes takes to be about 20 per cent.

Studies by this method in adrenalectomized dogs, allowed to show mild toxic symptoms by extract withdrawal are indicated in Table 2, and show a considerable shrinkage in interstitial fluid volume during adrenal insufficiency, and its expansion upon subsequent injection of the water and salt hormone. The circulation in these animals was well maintained, and they were not allowed to become seriously ill.

If this method, using thiocyanate, gives the volume of the water of the erythrocytes as well as that of the extracellular fluids, the error would occur in both the control estimation and in that made during the state of insufficiency. Both values, therefore, are probably too high, at least by the volume of water within the erythrocytes. If fluid enters the red blood cells as well as other cellular structures during insufficiency, the actual shrinkage of the extracellular fluid will be greater than the measured value, by this amount. The change in mean corpuscular volume, as noted (Table 2), 61.3 to 75.2 in one experiment, is very considerable. The blood changes would suggest a loss of about 20 per cent of the original volume of extracellular fluid, and substantiate reasonably well the values for shrinkage observed in

the thiocyanate measurement of the whole volume of extracellular fluid. The method is admittedly crude, but the magnitude of the observed changes makes them appear significant.

C. Recent studies made by Darrow and Yannet (15) on the redistribution of water and electrolytes which occurs after the intraperitoneal injection of isotonic glucose solution, in normal dogs, have a bearing upon the exchanges of body water which follow removal of the adrenals. After such an injection of glucose into the peritoneal cavity, an exchange of plasma electrolytes takes place into this artificial ascitic fluid. Capillary absorption of the injected peritoneal fluid does not appear to take place until an equilibrium is reached,

TABLE 2

Dog 160. Bilaterally adrenalectomized. Effect of withdrawal of hormone upon the interstitial fluid volume as measured by means of sodium thiocyanate

DATE	WEIGHT	CALCULATED INTERSTITIAL FLUID VOLUME	CALCULATED AS PER CENT BODY WEIGHT	BLOOD UREA	ERYTHROCYTES	HEMOGLOBIN	VOLUME PACKED ERYTHROCYTES	MEAN CORPUSCULAR VOLUME
1935	*kgs.*	*cc.*		*mgs.%*	*millions per cu. m.*	*gms. %*	%	%
Nov. 22	7.8	2,580	33.1	18	5.3	10.7	32.5	61.3
Cortical extract injections withdrawn								
Nov. 25	7.5	2,160	28.8	106	6.3	12.6	47.4	75.2
Typical symptoms of insufficiency, but with fair pulse. Slight diarrhea. Extract injections resumed								
Nov. 29	7.7	2,490	32.3	21	5.5	10.4	31.0	56.4

which does not occur for some hours. If the ascitic fluid is withdrawn at an earlier period, say about 5 hours after injection, an approximate recovery of the whole original volume is possible, and it is found that the fluid contains, by calculation, from 10 to 35 per cent of the total body sodium, an amount of the same order as that lost in adrenal insufficiency. Since practically no urine is voided during this period, a situation is created in which, essentially, only sodium and chloride are withdrawn from the body without gain or loss in the total amount of body water. The observed result is a marked hemoconcentration which the authors ascribe to a shift of fluid from the plasma and interstitial spaces into the tissue cells themselves. Darrow and Yannet drew attention to the analogy between this condition and that

TABLE 3

Dog 148. Intraperitoneal glucose experiment

No food nor fluids given during the course of the experiment. Normal animal with intact adrenals

DATE	WEIGHT	PLASMA NPN	PLASMA SODIUM	PLASMA POTASSIUM	PLASMA CALCIUM	PLASMA CHLORIDE	CARBON DIOXIDE	PLASMA PHOSPHATE	PLASMA PROTEIN	RBC	HEMOGLOBIN	VOLUME PACKED RBC	URINE VOLUME	SODIUM OUTPUT	POTASSIUM OUTPUT	NITROGEN OUTPUT
1934	*kgs.*	*mgs.%*	*m.eq./l.*	*m.eq./l.*	*m.eq./l.*	*m.eq./l.*	*m.eq./l.*	*m.eq./l.*	*gm.%*	*million/ c.cm.*	*gm.%*	*%*	*cc.*	*m.eq.*	*m.eq.*	*m.eq.*
Sept. 28 10 a.m.	12.5	36	144.4	4.2	4.6	110.8	24.3	0.9	6.5	4.8	10.8	39.0				
						Given 937 cc. 5.5 per cent glucose intraperitoneally (75 cc./kg.)										
3 p.m.		33	132.2	3.8	5.6	97.5	23.1	1.2	7.9	6.2	14.0	45.0	30	0.4	1.8	0.03
						985 cc. fluid withdrawn from peritoneum, just after the blood sample at 3 p.m.										
Sept. 29 10 a.m.	11.6	32	138.2	3.8	6.2	101.0	22.0	2.0	7.0	5.5	12.3	41.3	480	Trace	6.6	1.9
Sept. 30 10 a.m.	11.4	32	139.1	3.6	6.0	102.2	24.0	1.1	7.0	5.7	12.5	41.2	180	4.4	4.4	3.7
						Dog in good condition. Walks without spasticity										

The ascitic fluid contained in milliequivalents per liter, 123.0 of sodium, 3.4 of potassium, 3.0 of calcium.

of adrenal insufficiency, and Gilman (16), in further studies, has shown the fall in blood pressure, the rise in plasma osmotic pressure, and the marked sensitiveness of dogs thus treated with glucose intraperitoneally, to the withdrawal of comparatively small quantities of blood, just as has been found to be the case in adrenal insufficiency.

It will be noticed, however (Table 3), that the parallelism is not quite exact, since the rise in plasma potassium and non-protein nitrogen concentration, so constant in experimental adrenal insufficiency, does not usually occur, nor are the clinical symptoms shown by the animal more than superficially suggestive of adrenal insufficiency. If the study of the blood plasma concentration is repeated over the next two days, after removal of the ascitic fluid, (both food and all fluids being withheld), no further change may be noted, and in fact a redilution of the blood plasma may actually occur, as observed in the lowered concentration of the hemoglobin, hematocrit, red blood cell count and plasma proteins, but associated with an actual increase in the concentration of plasma sodium. This, it may be remarked, is always accompanied by a considerable excretion of urine—after the removal of the ascitic fluid, in one particular experiment (Dog 148) of 480 cc. during the next 18 hours.

The simplest explanation of such an apparent redilution of the blood seems to be that all of the stores of extracellular fluids are not drawn upon in these acute experiments of short duration. Equilibrium is reached only after some hours with outlying depots of interstitial fluid, which then contribute their share of water and of sodium, diluting the concentrated plasma, and raising its sodium content. Stores of interstitial fluid, particularly in the connective tissue, at a distance from blood vessels or lymphatics, may be available for this purpose. The situation is analogous to that seen in diabetic patients who have lapsed rapidly into diabetic coma. The observed hemoconcentration seems much greater than the apparent loss of tissue hydration. Such patients require relatively much less fluid to overcome the toxic symptoms and hemoconcentration than do those whose acidosis has developed more slowly and with more thorough depletion of the fluid stores outside of the blood.

In order to test this possibility of replenishment of the plasma from outlying reservoirs of fluid to be found in the interstitial spaces, the

TABLE 4

Dog 165. Intraperitoneal glucose experiment

No food nor fluids given during the course of the experiment. Normal animal with intact adrenals

DATE	WEIGHT	TEMPERATURE	PLASMA NPN	PLASMA SODIUM	PLASMA POTASSIUM	RBC	HEMOGLOBIN	VOLUME PACKED RBC	PROTEIN	URINE	
1934	*kgs.*	*°F.*	*mg.%*	*m.eq.*	*m.eq.*	*millions /c.mm.*	*gms.%*	%	*gm.%*	*cc.*	
Dec. 5 9:30 a.m.	13.3	101.3	32	146.6	5.5	8.5	15.2	46.0	5.6		Determination of interstitial water by sulphocyanate method 3760 cc. = 29.6 per cent of body weight
					Given 998 cc. of 5.5 per cent intraperitoneal glucose (75 cc./kg.)						
3 p.m.	12.7	98.6	48	136.6	5.5	10.5	18.4	61.0	8.4	12	Stool and slight vomitus at 11 a.m. Appears very weak, but no spasticity
					970 cc. fluid withdrawn from peritoneum. Sodium 116.7 m.eq./l.						
Dec. 6 9:30 a.m.	12.2	100.8	70	138.7	5.9	9.5	17.8	55.7	7.2	165	Fairly active. No spasticity
					Given 610 cc. of 5.5 per cent intraperitoneal glucose (50 cc./kg.)						
3 p.m.	11.9	98.8	84	130.4	9.2	11.0	20.0	61.2	8.5	90	Very spastic. Skin folds inelastic. Hyperactive deep reflexes. The cramps of the leg muscle were intermittent and stimulated by movement or manipulation
					640 cc. fluid withdrawn from peritoneum. Sodium 101.0 m.eq./l.						
Dec. 7 9:50 a.m.	11.4	98.3	156	132.3	11.8	10.7	19.8	59.8	8.5	148	Slight spasticity; "weaving gait." Hyperactive reflexes. Skin folds inelastic. Determination of interstitial water by sulphocyanate method 2250 cc. = 19.7 per cent of body weight

Repeated injection of glucose intraperitoneally caused a loss of 179 m.eq. of sodium. Both the clinical condition of the animal and the blood pattern found closely resembled that observed in adrenal insufficiency.

original experiment was further extended (Table 4), on the day following the first intraperitoneal injection of glucose, by a second injection, again with subsequent removal of the ascitic fluid formed, after five hours, in order to exhaust further the supplies of interstitial electrolytes and fluid. In this instance on the morning following the second intraperitoneal glucose treatment the condition of the animal showed closer resemblance to the typical clinical picture of insufficiency in the adrenalectomized dog. The electrolyte pattern of the plasma, in all particulars studied, was identical, in this animal with intact adrenal glands, with that seen in the adrenalectomized animal allowed to go into insufficiency by withdrawal of injections of the cortical hormone. He had a spastic gait, hyperactive reflexes, low body temperature, irregular pulse and marked bradycardia. The inelastic skin folds and the lack of tone of the subcutaneous tissues characteristic of severe adrenal insufficiency in the dog were present. The rise in plasma potassium and non-protein nitrogen, as well as the fall in plasma sodium and chloride, are strictly comparable to the changes found in adrenal deficiency. In this intact animal these plasma changes appear to result from the more complete exhaustion of the supplies of interstitial fluid. The changes in interstitial fluid volume as measured by the thiocyanate method (Table 4) also support this assumption.

This model experiment in the normal animal with intact adrenals suggests strongly that the rise in plasma potassium and non-protein nitrogen, noted in adrenal deficiency, is not due to the removal of some direct influence of the cortical hormone upon the general permeability of cellular membranes. The plasma changes noted on removal of the influence of this water and salt hormone rest, we believe, primarily upon a renal retention of potassium and nitrogen which is coincidental with the increased renal excretion of sodium (7). It is duplicated in the intact animal treated with intraperitoneal glucose only when the dehydration of the interstitial fluids is sufficient in degree to produce interference and breakdown of cellular metabolism as well as to impede urinary excretion. Potassium is released but its renal excretion is impeded.

The process by which the blood reverts toward its normal condition of hydration in these experiments on fasting and thirsting intact animals is much the same as that observed during the recovery phase

after the injection of cortical hormone in the adrenalectomized dog. An excretion of urine occurs after removal of the peritoneal fluid. In this the concentration of sodium is very low. Potassium retention does not occur in the intact animal, except in the extreme condition of dehydration which has just been described, because, in the presence of the functioning adrenals, this base is readily excreted through the urine.[3]

The question arises in connection with increased sodium loss, both in the adrenalectomized dog, by way of the kidney, and in the normal animal treated with intraperitoneal glucose, as to why the resulting water shift which causes the dehydration should take place into the tissue cells. Simple urinary excretion of the excess of fluid would be anticipated, an assumption which we made in an earlier paper (5). At present we see no satisfactory answer to this question, and doubtless speculation is not justified. Other conditions associated with the urinary excretion of base (*e.g.*, ammonium and calcium chloride acidosis, diuretin diuresis, diabetic acidosis, cardiac diuresis, and the spontaneous diuresis of nutritional edema), have usually displayed a significant loss of potassium as well as of sodium, and with it an increased excretion of water. In adrenal insufficiency, however, as we have shown elsewhere (7), an actual potassium retention frequently takes place.

If water actually moves from the interstitial fluid into the cells it might be supposed that tissues such as muscle would increase in water content and that histological examination might even show a gross enlargement or distortion of cellular morphology. The most readily observed isolated cellular structure, the erythrocyte, as we have indicated above, does show such changes in volume as determined by the relation of the volume of packed red cells to cell count during adrenal deficiency. When it is recalled, however, that the probable volume of the intracellular water is two or three times that of the extracellular water (15), it will be seen that per unit a given loss from

[3] The injection of intraperitoneal glucose into a dog from which one adrenal had been removed produced a result more nearly resembling adrenal insufficiency than in the intact animal. In this case, dilution of the plasma and rise in the concentration of plasma sodium were delayed until the day after the removal of the ascitic fluid (Table 5).

TABLE 5

Dog 157. Intraperitoneal glucose experiment

No food nor fluid given during the course of the experiment. Right adrenal removed June 18, 1935. Left adrenal gland intact

DATE	WEIGHT	PLASMA UREA	PLASMA SODIUM	PLASMA POTASSIUM	PLASMA CHLORIDE	PLASMA PROTEIN	RBC	HEMOGLOBIN	VOLUME PACKED RBC	URINE VOLUME	SODIUM OUTPUT	POTASSIUM OUTPUT	NITROGEN OUTPUT	PHOSPHATE OUTPUT
1935	*kgs.*	*mgs.%*	*m.eq./l.*	*m.eq./l.*	*m.eq./l.*	*gms.%*	*million/ c.cm.*	*gm.%*	*%*	*cc.*	*m.eq.*	*m.eq.*	*m.eq.*	*mgs.*
Nov. 5 9:30 a.m.	15.2	12	145.9	5.0	111.8	6.3	7.0	15.3	46.2					
	Given 1140 cc. 5.5 per cent glucose intraperitoneally (75 cc./kg.)													
3:00 p.m.		15	132.8	4.5		8.5	8.4	16.9	62.2	22	1.9	Trace	0.4	14
	1280 cc. fluid withdrawn from peritoneum just after the blood sample was removed at 3 p.m.													
Nov. 6 9:30 a.m.	14.4	37	131.2	5.4	95.4	7.4	8.1	16.1	59.9	67	0.3	4.1	0.7	73
Nov. 7 9:30 a.m.	14.0	41	135.1	5.2	97.4	7.9	7.1	15.7	50.1	285	1.7	17.9	7.7	512
	Dog quite active. Walks and runs well													

The ascitic fluid contained in milliequivalents per liter, 103.8 of sodium, 2.5 of potassium, 87.0 of chloride.

the latter will increase the volume of the former by but one-half or one-third. Such changes in volume would be still less evident in a microscopic section which only reveals the changes on the plane surface.

Britton and Silvette (20) reported an actual increase in the water content of muscle tissue and liver tissue in the rat and in the cat in adrenal insufficiency. We have been unable to establish such changes in the water content of either rat or dog muscle, or liver (21), which we have believed beyond the limits of experimental error. It must be recalled that the impossibility of securing tissue specimens which do not contain interstitial fluid must serve to introduce very large and uncertain errors in such measurements.

SUMMARY

1. Evidence is presented (a) from balance experiments and blood studies upon animals recovered from adrenal insufficiency by means of injections of cortical hormone alone without added salt or fluids; (b) from direct measurement of approximate interstitial fluid volume during adrenal insufficiency by means of sodium thiocyanate; and (c) from experiments on intact animals in which sodium has been withdrawn without loss of water by means of intraperitoneal injections of glucose, concerning the shifts in the location of body water which occur as a result of withdrawal and of subsequent reinjection of the water and salt hormone of the adrenal cortex.

2. The conclusion is drawn that an actual shrinkage of interstitial fluid volume occurs during insufficiency, and that this volume is restored as a result of reinjection of the hormone. The principal movement of this fluid is into the cells, following withdrawal of the extract, and from the cells to the interstitial spaces when the hormone is reinjected.

3. It is probable that the blood concentration noted in adrenal insufficiency is due to three factors: (a) movement of extracellular fluid into the tissue cells, (b) drainage of plasma water into the extracellular fluid outside of the vascular system, and (c) augmented excretion of urine. Of these factors, the first is the most important.

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THE WATER AND SALT HORMONE OF THE ADRENAL CORTEX[1]

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One year ago we reported the successful maintenance of a group of totally adrenalectomized dogs over extended periods by the administration of adequate amounts of sodium chloride and sodium bicarbonate (1). During these experiments the animals were kept in a normal condition as regards appetite, activity and the maintenance of body weight. At the end of a period of study which varied from three to five months, adrenal insufficiency was produced when the salt feedings were withdrawn. An inverse relationship was found in these animals between the concentration of plasma sodium and potassium. This was demonstrated in studies of the plasma electrolyte pattern, made at frequent intervals following the administration of varying amounts of sodium chloride and sodium bicarbonate. When the plasma concentration of sodium fell below the ordinary value, due to withdrawal or inadequate dosage of sodium salts, the concentration of potassium rose. When sufficient sodium salts were then given to such animals, the abnormally high level of potassium fell, often to the normal values. This fall in the plasma concentration of potassium and of urea was

[1] The term "water and salt hormone" of the adrenal cortex was first employed by Long and Lukens (2). We have adopted this designation because it seems to describe adequately our present state of knowledge concerning this substance; it avoids confusion; and it leaves clearly as an open question the possibility of the presence of other hormonal principles in the adrenal cortex which may or may not be related to the one at present under discussion.

[2] The technical assistance of Miss Margaret Strauss, Harry Eisenberg, Mrs. Florence White, Irving Miller and Miss Regina Weistock is acknowledged. Our late co-worker, Dr. Read Ellsworth, performed the first potassium determinations made in this laboratory in the study of the function of the adrenal cortex.

associated with an increased urinary excretion of these substances, frequently with well-marked diuresis. The practicability of sustaining adrenalectomized dogs over prolonged periods by means of sodium salts, in which the concentration of sodium exceeded that of chloride, was confirmed shortly afterwards by Allers (3).

More recently (4) we have shown in balance experiments upon adrenalectomized dogs eating a meat diet, that changes in the potassium and nitrogen metabolism take place following the withdrawal of injections of the cortical hormone which are quite as striking as those occurring in the sodium balance, as previously described by Loeb (5) and subsequently by ourselves (6). When sodium is lost during the course of adrenal insufficiency, potassium is held back, but when the water and salt hormone, or a sodium salt in proper quantity, is again administered to such animals, urinary excretion of potassium occurs, associated with sodium retention. These changes last but a day or two when adequate therapy is instituted, and the animal is quickly restored to a normal state.

The appearance of severe toxic symptoms in the adrenalectomized dog, in our experience, is nearly always associated with a distinct rise in the concentration of plasma potassium, although experiments may be devised, as has been indicated previously (1), particularly by restricting the fluid intake, in which the plasma concentration of sodium is not lowered, but is, indeed, distinctly raised. By forcing fluids, without salt, on the other hand, the usual rise in plasma urea may also be prevented or considerably modified.

The effect of restricting or of forcing the intake of sodium salts upon the retention or excretion of potassium in the adrenalectomized dog naturally brings up the complementary question of the influence which increased or diminished potassium intake may exert upon the retention of sodium. The following experiments were designed to throw light upon the first phase of this problem.[3] (Tables 1 and 2.)

[3] The methods employed in this laboratory for the selection, preparation, care, and feeding of adrenalectomized male dogs, which were used exclusively in these experiments, have been previously described (7, 8). The conduct of metabolism experiments upon adrenalectomized dogs and the methods employed in chemical analyses of the blood, food and excreta have also been given elsewhere in detail (4, 6). The preparation of the cortical hormone used was manufactured in this

On a constant diet and intake of fluid and sodium chloride, and with a maintenance injection of cortical hormone which is barely effective, an increased intake of potassium in the adrenalectomized dog is associated with an increased output of urinary sodium and varying retention of potassium. The familiar changes in the plasma electrolyte picture eventually occur, when such doses of potassium salts are given, and toxic symptoms finally appear. When sodium salts are then given instead of potassium, the latter is lost and dilution of the blood takes place. The effect of a diet low in potassium content is apparently beneficial to the adrenalectomized dog, and less sodium salt, or salt and water hormone, is then required for maintenance according to recent observations by Allers, Nilson and Kendall (9). We have not succeeded in confirming this observation because we have not been able to carry out metabolism experiments consistently upon adrenalectomized dogs receiving a diet very low in potassium.

The quantitative relations of sodium and potassium intake in the diet to the retention and excretion of these elements in the animal body were studied by Bunge in 1873 (10). This author attributed the craving of herbivorous animals for common salt to the excess of potassium in the vegetable ration. He suggested that this excess of potassium was rapidly excreted in the urine, carrying sodium and chloride with it, because of some hypothetical interchange of anions between the two bases within the body. He showed in experiments upon himself that the addition of potassium phosphate or citrate (about 12.5 gms. potassium) to his diet, increased for a day the renal elimination of potassium, sodium and chloride. The equivalent sodium excretion in one experiment was considerably greater than that of chloride. On the following day, when no potassium was given, the excretion of urinary sodium and chloride was distinctly less than that of the control period. The effect of continued administration was not investigated, and although Bunge mentioned other omissions in his study, he built upon it an hypothesis which has been widely accepted for sixty years to explain the desire of herbivorous animals for common salt. In neither Bunge's study nor in that of Meyer and Cohn (11), who found that potassium bicarbonate in two-day periods produced a negative sodium and chloride balance, was it deter-

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laboratory by the method of Swingle and Pfiffner. We are indebted to Dr. Oliver Kamm of Parke, Davis and Co., Detroit for supplying us with adrenal glands for this purpose for the past several years. The Upjohn Co., Kalamazoo, Mich. has also furnished us with generous supplies of their preparation of the adrenal cortical hormone. These experiments are representative of several, in which the results are concordant.

TABLE 1

Dog 166. Effect of potassium chloride on the adrenalectomized dog sustained with water and salt hormone

The gain in weight and the return of the plasma sodium concentration to a normal level between April 3 and 8 indicates that the dosage of cortical hormone and sodium chloride upon the constant mixed diet was adequate. The dog was so maintained from April 8–13. The daily addition of 2 gms. potassium chloride then produced a partial drop in plasma sodium level April 18. 4 gms. potassium chloride then precipitated severe insufficiency and eventual death in 5 days with marked hemoconcentration. The effect on chloride was much less, presumably because this was continually supplied (as potassium chloride).

DATE	WEIGHT	RATION	PLASMA UREA	PLASMA SODIUM	PLASMA POTASSIUM	PLASMA CHLORIDES	BLOOD SUGAR	RED BLOOD CELLS	HEMOGLOBIN	HEMATOCRIT	PROTEINS
1936	*kgs.*		*mgs./100 cc.*	*m. eq./l.*	*m.eq./l.*	*m.eq./l.*	*mgs.%*	*millions per cu. mm.*	*gms.%*	*% red blood cells*	*gms. %*
Apr. 3	11.4	Mixed diet	28	136.9	4.7	109.5					
		0.5 cc. cortical extract +6 gms. sodium chloride daily									
Apr. 8	11.8	do	23	143.0	5.1	109.5	92	4.6	10.4	32.8	5.8
13	12.0		23	142.8	4.9		79				
		+2 gms. potassium chloride daily									
18	11.8	do	20	138.0	5.3	107.3	83			35.8	5.7
		+4 gms. potassium chloride daily									
23	11.1		75	131.3	6.2	103.6	86	7.2	14.4	47.2	6.7

Dog died four hours after this estimation.

TABLE 2

Dog 157. Effect of potassium chloride on the adrenalectomized dog sustained with water and salt hormone

Diet of 450 gms. lean meat and 500 cc. distilled water by stomach tube, in divided doses, 3 cc. cod liver oil, 1 gm. sodium chloride and 0.5 gm. calcium phosphate daily throughout the experiment. Administration of 4 gms. potassium chloride by stomach tube daily to the adrenalectomized dog in balanced condition produced an immediate loss of sodium and retention of potassium. At the end of the fifth day (Period 4) some food was refused (60 gms.) and the electrolyte pattern showed characteristic changes, with concentration of the blood. The administration of potassium chloride was stopped and 8 gms. sodium chloride + 2 gms. sodium bicarbonate were substituted. This in turn produced sodium retention and potassium excretion, with dilution of the blood.

PERIOD	DURATION OF PERIOD	WEIGHT	CORTICAL EXTRACT PER DAY	SODIUM BALANCE PER DAY	CHLORIDE BALANCE PER DAY	POTASSIUM BALANCE PER DAY	NITROGEN BALANCE PER DAY	PLASMA SODIUM	PLASMA CHLORIDE	PLASMA POTASSIUM	PLASMA NON-PROTEIN NITROGEN	RED BLOOD CELLS	HEMOGLOBIN	HEMATOCRIT	PLASMA PROTEIN
	days	*kgs.*	*cc.*	*m.eq.*	*m.eq.*	*m.eq.*	*gms.*	*m.eq./l.*	*m.eq./l.*	*m.eq./l.*	*mgs. %*	*millions per cu. mm.*	*gms.%*	*% red blood cells*	*gms. %*
1	3 control	14.6	2	+1.4	+0.9	−0.5	+1.0	143.2	108.1	4.6	33.3	5.8	13.1	44.6	6.1
				4 gms. potassium chloride given daily by stomach tube											
2	2	14.5	2	−10.1	−1.1	+6.2	−0.5								
3	2		2	−9.1	−0.4	−1.1	−0.8								
4	1	14.2	2	−7.8	−1.5	−3.2	−1.1								
								131.1	103.2	6.9	85.4	7.1	14.6	49.5	6.9
				8 gms. sodium chloride + 2 gms. sodium bicarbonate by stomach tube. Potassium chloride discontinued											
5	1		2	+3.0	−0.8	−12.1	−3.2								
6	2	14.5	2	+4.8	−2.0	−4.1	−0.9								
								139.8	107.7	5.1	38.3	6.1	13.6	45.1	5.8

mined whether continued use of potassium salts would produce a serious depletion of body sodium. Hart and his co-workers (12) concluded that the magnitude of potassium intake did not influence sodium chloride consumption or its retention in stock animals. Gerard (13) in rather short balance studies on dogs and mice thought he obtained evidence that potassium salts drive out sodium.

Biernacki (14), while confirming the studies of Bunge, stressed the rôle of potassium rather than that of its salts.

Miller (15), in experiments upon pigs, found that a large proportion of potassium added to a constant diet was eliminated within 48 hours of its ingestion, and that a discharge of sodium and of chloride accompanied it. If the augmented potassium intake was continued, however, the quantities of sodium and chloride daily excreted gradually became smaller. The normal pig could conserve its sodium and chloride in spite of the ingestion and excretion of large quantities of potassium, and the animal could retain sodium successfully if the high potassium intake continued. He concluded that the organism has a means of keeping the sodium and potassium content of the blood constant in spite of variations in the food supply.

The intravenous injection of potassium chloride increased the output of sodium in the normal female dog, according to Whelan (16), and sodium chloride caused an increased excretion of potassium, particularly in man. She found that the concentration of potassium in the urine of the dog is normally higher than in man and that it rises more sharply after sodium chloride injection. These were also acute experiments.

Bassett, Elden and McCann (17) found no increased sodium loss during a period of increased potassium intake in two normal men, although the major portion of the potassium was excreted in the urine. The dose of potassium citrate given, (3–4 grams potassium per day), was less than the amount taken by Bunge (12.5 grams per day) and no influence on weight was noted. However, the five-day periods used were too long to avoid the masking of any immediate effect. Loeb and his co-workers (18) noted that potassium chloride given to a normal person caused a slight increase in total base excretion. They made the important observation that potassium passes through the kidney under ordinary circumstances with greater facility than either sodium or chloride. Loeb was the first to comment upon the curious reversal of this effect in the adrenalectomized dog (5).

Mackey and Butler (19) made a distinction between two normal subjects following the ingestion of 5 grams of potassium chloride. One subject on a liberal sodium chloride intake excreted the extra potassium promptly, whereas another subject on a low salt intake did not, and indeed showed a positive potassium balance during the entire period that potassium chloride was taken. In the first subject (liberal sodium chloride intake) the potassium chloride produced a negative sodium balance for the first two days in which it was given, but sodium was retained during the remaining four. A sufficient amount of sodium was held during the last two days to compensate the original loss entirely.

Blum and his co-workers (20), in man, found that the percentage of potassium in the blood rose while that of sodium fell after the administration of potassium. They believed the resulting diuresis was due to the excretion of sodium, which they considered the regulatory agent in water exchange. The diuretic action of potassium, according to this theory, is the consequence of the displacement of sodium by potassium in the body fluids. Retention of sodium was followed by increase in weight, and excretion of sodium was attended by weight loss. Most authors have recorded no consistent rise in serum or plasma potassium after its oral ingestion.

Keith and Binger (21) found that potassium is concentrated to a greater degree than sodium by the normal kidney. Even with diuresis the normal kidney excretes a urine in which the potassium concentration may be about fifty times that found in the serum. Potassium salts are promptly absorbed and readily excreted. Normal persons seem to tolerate relatively enormous doses without untoward effects. Thus Keith and Binger report the ingestion of 871 grams of potassium salts (358 grams potassium) during sixty-eight days without toxic symptoms. The prolonged use of huge doses of potassium iodide, as in the treatment of syphilis, may not produce untoward effects. Keith and Binger state that Bunge found that Irish laborers on potato diets, and African tribes on native foods, may take without detriment as much as 50 grams of potassium per day over long periods. In contrast, the average daily potassium ration in an ordinary mixed diet is 3 to 5 grams. No symptoms suggestive of sodium deprivation have been reported under these circumstances of large potassium intake in persons without adrenal disease.[4] An important factor of safety is doubtless the rapid excretion of excess of potassium by the normally functioning kidney.

There is a considerable literature on the opposite question, namely, the effect of increased sodium ingestion upon potassium excretion. Much of it, however, is inconclusive. Richards, Godden and Husband (22) found that the addition of large amounts of sodium chloride to the diets of growing pigs caused an immediate increase in the urinary potassium which was practically balanced by diminished fecal potassium. This remarkable result, which is quoted frequently, would appear to suggest that the addition of sodium chloride to the diet of these animals facilitates the absorption of foods containing potassium. Addition of potassium citrate to the basal ration was found by these authors to cause the excretion of chloride but not of sodium. They concluded that their results did not support Bunge's theory of sodium impoverishment as a consequence of potassium feeding.

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[4] The symptoms reported by Arden (Australian J. Exper. Biol. & Med. Sci., 1934, 12, 121) following the ingestion of 15 gms. of potassium chloride cannot be considered similar to those of sodium deprivation such as have been recently reported by McCance in man. (Proc. Roy. Soc. London. Series B, 1936, 119, 245.) The one point of significant and striking likeness was the loss of muscular power and fatigue.

It is well recognized that the manner of excretion both of sodium and of potassium differs fundamentally from that of other inorganic elements of biological importance, such as calcium, magnesium, and phosphorus. The former are absorbed almost completely from the gastro-intestinal tract and are excreted in the urine together with various anions which may be available. Reliable studies have indicated that in man and dog, at least, the amount of potassium excreted by the bowel is fairly constant and comes from undigested food residue (17, 23). It is fortunate that fecal sodium and potassium excretion are thus of small importance compared to their urinary excretion. Were this not the case the attempt to trace metabolic changes in the daily balance such as we have reported would be rather hopeless.[5]

It is said that sodium may have a beneficial effect in potassium poisoning. Amberg and Helmholz (24) found that guinea-pigs which had previously received sodium chloride injections required a much larger lethal dose of potassium chloride or sulphate than those not so treated. The presence of 50 per cent glucose in the potassium chloride solution also increased the protection of the animals.

Greenwald (25) as well as Whelan (16) observed no alteration in the potassium content of serum following the intravenous injection of sodium chloride in dogs. Whelan also found a variable increase in potassium excretion in man after intravenous injection of sodium chloride. The potassium excretion exceeded that of sodium. Wiley *et al.* (26) found that the addition of 100 m.eq. sodium chloride daily to the diet of a normal man increased the output of urinary potassium for a period of three days. The fecal potassium remained constant. In a second period of three days, however, total potassium output nearly balanced its intake, fecal potassium increasing and urinary potassium becoming less. Sodium bicarbonate added to the diet affected potassium excretion very little at first, but later a potassium retention occurred.

In *summary*, the evidence regarding the effect of potassium salts upon sodium excretion in intact animals and normal human subjects appears to indicate that while the excretion of sodium, and perhaps more particularly of chloride, may be temporarily augmented, no sustained loss occurs. It is not possible in this manner to rid the body of any appreciable quantity of its sodium store. The converse effect of sodium salts upon potassium excretion in normal subjects appears to be that an increased excretion of potassium is produced in the first place, but this increase is not sustained. Its magnitude seems to depend somewhat upon the level of potassium intake. In the normal animal with intact adrenal glands, therefore, neither the feeding of large amounts of sodium nor of potassium will seriously deplete the body stores of either of these essential elements.

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[5] It is not uncommon for dogs on a meat diet to go without defecation for several days at a time. Attempts to apportion fecal sodium and potassium excretions accurately for one or two day periods under such circumstances are clearly impracticable.

The data which have been presented in this and in preceding papers indicate that the presence of the water and salt hormone is needed to maintain the concentration of potassium and sodium at a fairly constant and stable level in the body fluids. In the absence of this hormonal influence the normal electrolyte pattern becomes seriously distorted. With the mineral salt intake of the ordinary diet the potassium concentration usually rises and that of sodium diminishes. In the absence of adequate normal hormonal regulation, excess of potassium tends to drive out sodium. On the other hand, if sodium intake is sufficiently increased and potassium intake is not excessive, the electrolyte pattern is more nearly restored. In the absence of the hormone, however, the deficiency is never quite completely repaired. As we have previously pointed out (1), "It is not to be expected that in the absence of this regulatory mechanism it should be possible to supply additional sodium and chloride ions in amounts just sufficient to repair the body deficit resulting from their uncontrolled excretion, and thus to permit the salt and water metabolism to be maintained with the efficiency which it possesses in the normal presence of the natural hormone."

The function of the water and salt adrenal cortical hormone has to do, we believe, with the regulation of sodium and potassium metabolism, including the adjustment and maintenance of the proper ratio between these ions as well as their total concentration in the body fluids. It enables the animal to absorb from the gastro-intestinal tract different amounts of sodium and potassium, in varying ratios, and still to control within a narrow range the quantities of either which are to be retained or excreted.

The accelerating effect of thyroid extract, and of fever and infection, upon the production of adrenal insufficiency in the adrenalectomized dog, and upon patients with Addison's disease, has been discussed in previous publications (7, 27, 28). Where inadequate reserves of the cortical hormone are available, toxic destruction of tissue proteins, with release of potassium, may render the animal more liable to adrenal insufficiency. In the absence of the water and salt hormone the excess of potassium is not readily excreted, as in the normal animal, whereas the excretion of sodium is facilitated. The recent study of McCance (29) upon sodium depletion in normal subjects

indicates that this effect is associated with tissue destruction and a negative potassium and nitrogen balance.

SUMMARY

The feeding of moderately large amounts of potassium in the form of potassium chloride to the adrenalectomized dog, previously maintained in balance with sodium chloride and cortical extract, on a constant food and water intake, causes an increased urinary loss of sodium and leads eventually to a condition of typical adrenal insufficiency. The added potassium tends to be retained, contrary to the effect in the normal dog with intact adrenal glands.

Increasing the intake of sodium chloride in the animal showing early symptoms of cortical insufficiency tends to lower the plasma potassium level and increases the urinary output of potassium, although not always effectively.

The adrenalectomized animal in the absence of the salt and water hormone is peculiarly sensitive to the proportions of ingested potassium and sodium salts; increased amounts of the one tend to drive out the other.

It is suggested that the unfavorable effect of thyroid extract or of infection on the adrenalectomized dog may be due in part to increased destruction of tissue protein, which releases nitrogen and potassium. These find less ready excretion in this animal, in the absence of the controlling influence of the salt and water hormone, but at the same time augment the excretion of urinary sodium.

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THE SURGICAL TREATMENT OF GASTRIC AND DUODENAL ULCERS

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The purpose of this paper is an attempt, through an analysis of the operative results obtained in a series of cases, to determine with as great certainty as possible the type of operation best suited to each individual patient who has a peptic ulcer.

Posterior gastro-enterostomy is discussed, since the technique of this operation forms the basis of all our procedures dealing with gastric and intestinal anastomoses.

Seven drawings are reproduced of illustrations from original articles to show the outstanding evolutionary steps in the development of the posterior gastro-enterostomy operation.

Eleven original drawings are given of the posterior gastro-enterostomy as it is now carried out in this clinic.

GASTRIC AND DUODENAL ULCERS

Two hundred and ninety-three (293) patients were operated on in the Johns Hopkins Hospital for ulcer of the stomach or duodenum in a period of nine years, from September 1, 1925, to August 31, 1934.

Duodenal ulcer	186	63.4%
Duodenal and gastric ulcer	2	.6%
Gastric ulcer at the pylorus	63	21.5%
Gastric ulcer at the cardia	2	.6%
Gastric ulcer at the lesser curvature	26	8.8%
Gastric ulcer at the greater curvature	2	.6%
Gastric ulcer at the posterior wall near the lesser curvature	3	1.02%
Marginal ulcer	7	2.3%
Jejunal ulcer	2	.6%
	293	99.4%

There were 254 males, 204 white and 50 black; and 39 females, 29 white and 10 black; the percentage of males in this series being 86.6%, and of females 13.3%.

The youngest patient was a white boy of 17 years, and the oldest a colored man of 78 years. Both sex and race groupings show the incidence to be most frequent in the 40–49 year decade and next in the 30–39 year decade, the first symptoms appearing, on an average, at a slightly younger age in the black than in the white race.

Chart A shows that on the average the patients at the time of operation were younger in the male group than in the female, and younger in the black race than in the white; 39.6 years for the black males, 42.9 years for the white males, 44.0 years for the black females, and 46.0 years for the white females.

CHART A

Age at operation

	TOTAL AGES	NUMBER OF CASES	AVERAGE AGE
			years
White males	8810	205	42.9
White females	1298	28	46.0
Black males	1980	50	39.6
Black females	440	10	44.0

Chart B gives a list of occupations of the patients who suffered from gastric or duodenal ulcer. It is difficult to draw any definite conclusions from so varied a list. Of the 278 patients whose occupations were noted, 120, or 43.1%, were engaged in heavy manual labor, 79, or 28.3%, in light manual labor, and 79, or 28.3%, in work other than manual labor. Another division of the same group shows that 152, or 54.6% pursued outdoor occupations, and 126, or 45.3%, indoor occupations.

Chart C gives a list of all the types of operations done in this group of ulcer cases and we have arbitrarily subdivided these into five groups in order to facilitate their individual study.

In group 1 (C) are put all those patients in whom a new opening was made between the stomach and the jejunum. The perforated ulcers in which a gastro-enterostomy was performed are not included in this

CHART B

Occupations of patients with gastric and duodenal ulcers

Accountant	1	Golf club worker	1	Plumber	3
Advertising manager	1	Grocer	3	Policeman	1
		Guard, City Jail	1	Porter	1
Barber	2				
Barrel-maker	1	Helper on truck	1	Railroad ticket agent	1
Blacksmith	3	Houseman	1	Real estate agent	2
Boiler-maker	1	Housewife	27	Restaurateur	1
Boiler-tender	1	Huckster	1	Retired	1
Box factory worker	1			Rolling mills worker	1
Box-maker	1	Insurance agent	2	Runner of sanding machine	1
Bricklayer	1				
Brakeman	2	Janitor	1		
Broker	1			Safety director	1
Business executive	2	Laborer	31	Salesman	7
Butcher	2	Lawyer	4	Seaman	2
Butler	3	Lumber worker	2	Secretary	1
				Service Station worker	2
Cabinet maker	2	Machinist	6	Signal man	1
Carpenter	4	Mail carrier	1	Steel worker	2
Chauffeur	4	Manager	1	Stenographer	2
Chemist	2	Marine	1	Stevedore	6
Circulation Department (newspaper)	1	Mechanic	1	Storehouse keeper	1
Clerical workers	10	Merchant	1	Store-manager	1
Coal business	1	Milk salesman	1	Street cleaner	3
Collector	1	Mill worker	1	Student	2
Conductor	1	Miner	1	Supt. of Public Sewers	1
Contractor	4	Moulder	1		
Cook	6			Tailor	10
		Night watchman	1	Telephone helper	1
Day worker	1	Nurse	2	Textile worker	1
Domestic	1	Nurseryman	1	Tobacco grower	1
Dressmaker	1	None given	15	Trainman	1
				Trucker	2
Electrician	4	Orderly	6		
Engineer	4			Upholsterer	2
Expressman	1	Painter	5	U. S. Customs Service	1
		Paperhanger	1	United States Navy	1
Farmer	21	Paper-mill worker	1		
Foreman	2	Peddler	1	Veterinary Surgeon	1
		Physician	4		
Garage man	1	Pipe-fitter	1	Waiter	2
Gardener	1	Plasterer	1	Wood-worker	1
				Wool-treater	1

CHART C

OPERATIONS	NUMBER OF CASES
Group 1	
Posterior Gastro-enterostomy (This group includes Simple Posterior Gastro-enterostomy,) 131; Posterior Gastro-enterostomy with Appendectomy, 14; Posterior Gastro-enterostomy with Cholecystostomy, 3; Posterior Gastro-enterostomy with Cholecystectomy, 1; Posterior Gastro-enterostomy with Inversion of Diverticulum, 1	150
Anterior Gastro-enterostomy, Entero-enterostomy	14
Posterior Gastro-enterostomy, Entero-enterostomy	1
Pyloroplasty	15
Gastro-duodenostomy	4
Group 2	
Closure of Acutely Perforated Ulcer	30
Closure of Acutely Perforated Ulcer with Posterior Gastro-enterostomy	27
Closure of Ulcer from Inside	1
Bilateral McBurney Drainage for Perforated Ulcer	1
Cauterization and Closure of Perforating Ulcer	7
Group 3	
Partial Resection of Stomach with Posterior Gastro-enterostomy	6
Partial Resection of Stomach with Anterior Gastro-enterostomy, Entero-enterostomy	1
Wedge Resection of Stomach	4
Sleeve Resection of Stomach	3
Polya Resection of Stomach	1
Group 4	
Secondary operations on patients who had a previous operation done at some other hospital	19
Group 5	
Jejunostomy	4
Exploratory Laparotomy	5
Total	293

group as they present a different, distinct problem; neither are the cases in which a Billroth II or the Polya operation was performed. These appear in groups 2 (C) and 3 (C).

Group 2 (C) is a record of the acutely perforated gastric and duodenal ulcers, treated either by simple closure of the ulcer or by closure combined with a posterior gastro-enterostomy. This group also includes 7 cauterizations and closures of ulcers that were penetrating through the wall of the lesser curvature of the stomach but had not yet perforated.

Group 3 (C) includes the resections with and without a gastro-enterostomy; Group 4 (C) the secondary operations on patients who had been submitted to a previous stomach operation at some other hospital; Group 5 (C) the simple exploratory laparotomies and the jejunostomies.

The cases with a short-loop, posterior, gastro-enterostomy alone are first discussed, since this operation forms the basis of practically all the gastric operations done in this clinic. The three-layer continuous suture is the one generally employed in all gastro-intestinal anastomoses at the present time.

Of the 150 patients on whom this operation was done, 3 died, an operative mortality of 2%, 110 ran an entirely smooth and uneventful postoperative course, 22 vomited once to 3 times, 7 vomited 3 times or more, 4 had wound infection; there was 1 slight and 2 severe hemorrhages. Two of these patients had hiccups, 12 had pneumonia during the postoperative course, none had peritonitis, none had postoperative obstruction.

In estimating the final results in this group of posterior gastro-enterostomies, 116, or 77.3 % of the 150 patients, have either replied to letters or been examined personally; 34, or 22.6%, have not been located. Of these 116, 86, or 74.1%, are well, 16, or 13.7%, are improved, 1, or 0.8%, unimproved, and 13, or 11.2%, are dead.

Of the 13, or 11.2%, who died during the 10 years which have followed operation, 3 died immediately after operation, as stated before (two of bronchopneumonia and one of hemorrhage). Five of the 13 patients died of causes not related to the condition for which the gastro-enterostomy was done, and, therefore, might have been listed as *well*, having recovered from their gastric or duodenal complaint before death. Three of these 13 patients died with carcinoma of the stomach, one of tuberculous peritonitis, one of heart failure, one of lung abscess, one of pneumonia following repair of a ventral hernia, one of "causes

unrelated to his original ulcer", and one apparently of carcinoma of the head of the pancreas.

The only patient to develop obstructive symptoms following operation was the 13th in this group. A marginal ulcer was excised one year after his first operation and the gastro-enterostomy opening was closed. He later had a third operation done elsewhere and died, but the details of this are not available. This is the only patient who has had a marginal ulcer following a simple posterior gastro-enterostomy. This gives a total of 1, or 0.6%, in 150 cases. If, however, only the 116 traced patients are included, 1 marginal ulcer in 116 cases gives a percentage of 0.8%.

Fourteen anterior gastro-enterostomies for ulcers were done, with 3 operative deaths, a mortality of 21.4%. Thirteen of these patients have been traced, and of these, 7, or 53.0%, are well; 2, or 15.4%, improved; and 4, or 30.7% are dead (3 of these died just after operation).

Fifteen patients were submitted to a Finney pyloroplasty without an operative death. Of the 14 who were traced, 11, or 78.5%, are well, 2, or 14.2%, are improved, and 1, or 7.1%, unimproved.

Five patients were subjected to a gastro-duodenostomy without an operative death. Four have been traced and all are well.

The 58 patients with acutely perforated ulcers are listed in Group 2 of Chart D. Simple closure of the perforations was performed on 30 of this group; closure combined with a posterior gastro-enterostomy was performed on 27, and a bilateral drainage through a muscle-splitting incision was done in 1 case, thought to be a terminal pneumococcus peritonitis. The incidence of fatal postoperative bronchopneumonia is quite high in this group. Twelve of the 30 patients with an acutely perforated ulcer, on whom a simple closure of the ulcer was done, died —an operative mortality of 40.0%. Of these twelve, 3 had a spreading peritonitis, and 9 had a severe bronchopneumonia; 3 others had a bronchopneumonia, but recovered.

It is rather striking that only two of 27 with an acutely perforated ulcer on whom a posterior gastro-enterostomy was performed in addition to the closure of the ulcer died—a mortality of 7.4%. It is quite probable that the reason for the difference in mortality between the

groups is that the closure alone was performed upon the very sick patients. Many of the patients, however, on whom a posterior gastro-enterostomy was done as well as a closure of the ulcer were desperately ill, but had to have a new opening made on account of narrowing of the pylorus which followed closure.

Group 3 of Chart C contains 15 partial resections of the stomach for ulcer. Six of these were the Billroth II operations, 1 an anterior gastro-enterostomy and an entero-enterostomy with resection, 4 were wedge resections of the ulcer, 3 were sleeve resections of the stomach and 1 a Polya.

Of the 6 patients with a partial resection and posterior gastro-enterostomy, the Billroth II operation, all recovered from the operation. Of these, 4 have been traced, and all are well.

Of the 4 patients with a wedge resection of the ulcer, 1 died after operation, 3 have been traced and of these 1 is well, 1 is improved, and 1 is dead (postoperative bronchopneumonia). The patient with a Polya resection died 3 years after operation of lung abscess.

Group 4 of Chart C includes the 19 secondary operations performed on patients who had undergone a previous stomach operation at some other hospital. Seven patients in this group had a marginal ulcer, which in two had perforated the transverse colon.

Group 5 of Chart C lists 4 jejunostomies performed on patients with extensive ulcers. Two of these had large ulcers high up in the cardia, the remaining two had extensive scarring of the stomach and, in addition, a positive Wassermann. In this group also appear 5 exploratory laparotomies where nothing abnormal could be found.

Operative possibilities other than a posterior gastro-enterostomy in dealing with gastric and duodenal ulcers are (1) pyloroplasty, (2) gastro-duodenostomy, (3) anterior gastro-enterostomy with an entero-enterostomy, (4) simple excision of the ulcer, and, (5) partial resection of the stomach.

1. Pyloroplasty. In a certain percentage of cases with the ulcer just at the pyloro-duodenal junction and a duodenum that can be mobilized this has proved an excellent operation. The results show no deaths in 15 cases, 11 of the 14 traced patients are well, or 78.5%; 2, or 14.2% improved and 1, or 7.1% unimproved.

2. In 5 cases gastro-duodenostomy has been done. Of these patients 4 have been traced and found well. This operation is likewise limited in its application, mainly owing to anatomical difficulties.

3. An anterior gastro-enterostomy with an entero-enterostomy should be employed only when the posterior surface of the stomach cannot be reached either because of inflammatory changes or a short, thick transverse mesocolon.

4. Simple excision of the ulcer is usually inadequate and the original condition tends to recur.

5. Resection of the stomach with a posterior gastro-enterostomy, either the Billroth II or the Polya type, will be followed by an immediate mortality that is considerably higher than that of gastro-enterostomy. The results of these operations are, however, extremely satisfactory, and in doubtful cases in which it is difficult to differentiate between a carcinoma and a chronic ulcer, resection is indicated when the operation is feasible.

COMMENT

The conclusion reached in the analysis of the recent operative results of patients suffering from a pyloric or duodenal ulcer is that gastro-enterostomy is the operation that promises the most benefit to the patient in the large majority of cases, because of the low operative mortality, the smooth postoperative course, and the high percentage of favorable ultimate results.

It is often said that when patients are subjected to an operation on the stomach, no matter how good the ultimate result may be, they will have a stormy and uncomfortable postoperative course. As a matter of fact, there is no reason why they should have anything but the most comfortable sort of convalescence after this operation. In the 177 posterior gastro-enterostomy cases reported, 127 ran a perfectly smooth and uneventful postoperative course. Only 10 patients vomited more than 3 times, none were obstructed, there were two severe postoperative hemorrhages and one slight postoperative hemorrhage, and there was one case of peritonitis following closure of a perforated ulcer.

It is unfortunate that the term "vicious circle" was introduced into the surgical vocabulary, for it gives an incorrect idea of the nature of

the cause of some vomiting that occurs postoperatively. The so-called vicious circle is nothing but high intestinal obstruction. After having operated upon several of these cases, it became evident that one of the commonest causes of this high intestinal obstruction was a change in the mesocolon, usually from edema, which produced the obstruction. Such an obstruction could not have occurred if the mesocolon had been sutured high upon the stomach, so that from one and a half to two inches of the stomach projected into the greater peritoneal cavity. If the mesocolon had been sutured close to the line of anastomosis on the small intestine, such a change in the mesocolon would certainly have caused obstruction. The short loop suggested by Petersen obviated some of the causes of obstruction, but suturing the mesocolon high on the stomach is one of the principal factors in preventing postoperative high intestinal obstruction.

Jonnesco almost 50 years ago demonstrated that the duodenum may enter the greater peritoneal cavity in one of two ways. In almost 75% of the cases it passes through the root of the mesentery. When it enters the greater peritoneal cavity in this way, it is directed downward and to the left. In about 25% of the cases it runs in the lower leaf of the transverse mesocolon. It is then swung by a mesocolic band downward and to the right. It is best to leave the first portion of the jejunum in its natural position and attached to the stomach in accord with this position. Mayo in 1906, as is shown in the accompanying illustrations, held that the normal direction of the first portion of the jejunum lies downward and to the left, while Moynihan in 1905 claimed that it was downward and to the right. Lewis in 1909 referred to the teachings of Jonnesco in 1889 that in 75% of people the normal course is downward and to the left and in 25% it is downward and to the right. He therefore advocated approximating the jejunum to the stomach in accordance with the way in which it lies in each case.

The three-layer suture is most satisfactory. It provides hemostasis and an edge to edge approximation of the tissue, obviating pressure necrosis which of necessity must occur when any type of mattress suture, interrupted or continuous, is inserted through the mucous membrane. Such necrosis due to strangulation may lay the basis for a subsequent gastro-jejunal ulcer.

The success of the gastro-enterostomy operation, therefore, largely

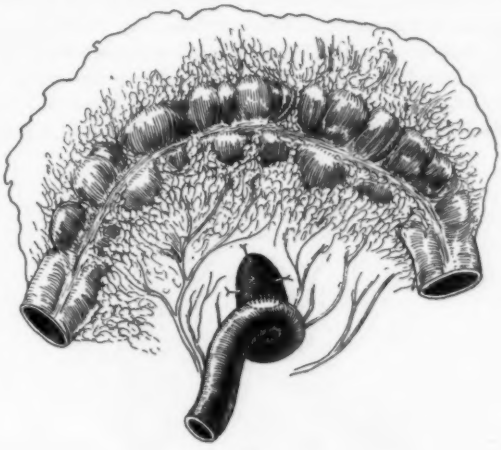
depends on the following technical considerations, (1) the pre-operative cleansing of the stomach, (2) the care in guarding against contamination during operation, (3) the approximation of the first portion of the jejunum to the posterior surface of the stomach in agreement with the anatomical position found in each individual case, (4) the suturing of the transverse mesocolon high up on the stomach wall back from the site of the anastomosis, (5) the accurate approximation of the mucosal edges, control of hemorrhage, avoidance of necrosis by means of the three-layer continuous suture, and (6) careful adherence to the other operative details of this operation as shown in the accompanying illustrations.

No extravagant claims are advanced for gastro-enterostomy. It is not a panacea for all gastric and duodenal ulcers. Nevertheless, it is felt that this operation may and should be applied in the majority of these lesions, occurring as they do in the pyloric portion of the stomach and the first portion of the duodenum, and that it is one of the most satisfactory operations in the armamentarium of the surgeon.

I

(After Wölfler, A.: *Cntrlbl. f. Chir.*, 1881, viii, 705–708)

This represents the first gastro-enterostomy, (anterior, ante-colic, long loop, retro-peristaltic), performed by Wölfler on September 28th, 1881, in Vienna at the suggestion of Nicoladoni, to relieve obstruction in inoperable carcinoma of the pyloric portion of the stomach.



II

(Hacker (von): *Arch. f. klin. Chir.*, 1885, xxxii p. 616–625)

Von Hacker in 1885 was the first to perform a posterior gastro-enterostomy, dividing the transverse mesocolon at a right angle to the long axis of the bowel. (Courvoisier had previously, in 1883, performed a posterior gastro-enterostomy, dividing the transverse mesocolon parallel to the long axis of the bowel, and gangrene of the transverse colon had resulted through injury to the middle colic artery.)

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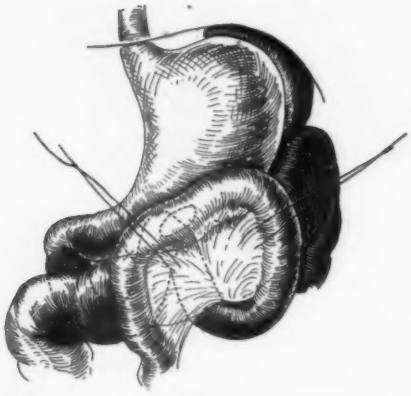
* These drawings were made from the original illustrations by Mrs. Frances Coleman Woodhall. Dr. John M. Olds gave valuable assistance in the compilation of the hospital records.

III

(Jaboulay: *Arch. Prov. de Chir.*, 1892, i, 1–22)

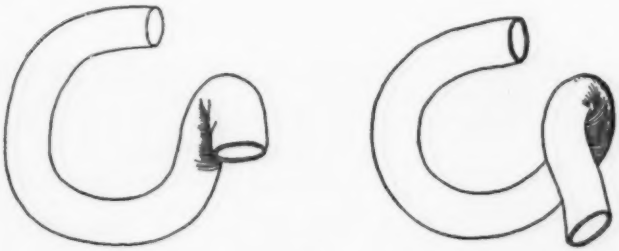
This represents the combination of an entero-enterostomy with a gastro-enterostomy, using a loop proximal and a loop distal to the site of anastomosis for this purpose. (Lausenstein, a year previously, in 1891, had suggested this procedure but made no definite suggestion as to which loops should be employed.) Previous to the introduction of the entero-enterostomy shown here, the anterior gastro-enterostomy with its necessarily long loop of bowel had almost always resulted in the so-called "circulus vitiosus," which, in reality is a high intestinal obstruction.



IV

(Doyen, E.: *Arch. Prov. de Chir.*, 1894, iii, 673–697)

Doyen was the first to employ a gastro-enterostomy on patients with a gastric or duodenal ulcer. (This was a long loop, ante-colic anastomosis.)



V

(Petersen, W.: *Beiträge z. klin. Chir.*, 1901, xxix, 597–616)

In 1900 Petersen described the two variations found at the duodeno-jejunal fold. His illustration shows that the first portion of the jejunum may point downward and to the left, or downward and to the right. He therefore advocated, in performing a gastro-enterostomy, not disturbing the anatomical position of the jejunum at this fold, but approximating it to the stomach in the position found in the individual case. (This is of especial significance in connection with the divergent opinions of Mayo and Moynihan.)

VI

(Moynihan, B. G. A.: Abdominal Operations, 1905, 156)

Moynihan believed that the normal direction of the first portion of the jejunum lies downward and to the right, and approximated the jejunum to the stomach accordingly.

VII

(Mayo, W. J.: *Annals of Surgery*, 1906, xliii, 537–542)

Mayo believed that the normal direction of the first portion of the jejunum lies downward and to the left. Therefore his first illustration shows the kink in the jejunum resulting from changing its direction, while his second illustration shows no kink in the jejunum when its normal direction is preserved.

TECHNIQUE OF GASTRO-ENTEROSTOMY EMPLOYED AT THE JOHNS HOPKINS HOSPITAL*

FIG. I. Shows the rent in the transverse mesocolon made at a right angle to the long axis of the bowel in order to avoid injuring the middle colic artery. The posterior surface of the stomach may be seen presenting through this rent.

* The drawings were made at the time of operation by Miss Angela Bartenbach.

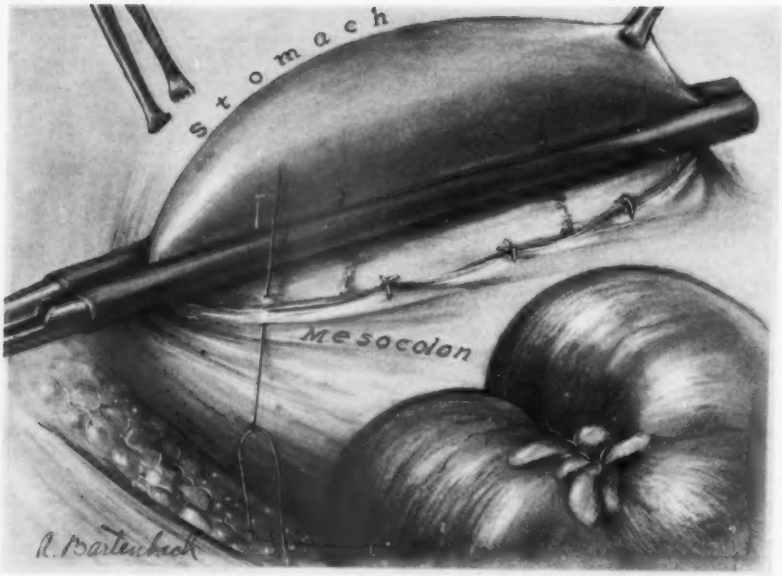


FIG. II. The posterior surface of the stomach has been pulled through the rent in the transverse mesocolon, and interrupted stitches of catgut are now taken to fix the edge of the rent to the posterior surface of the stomach.

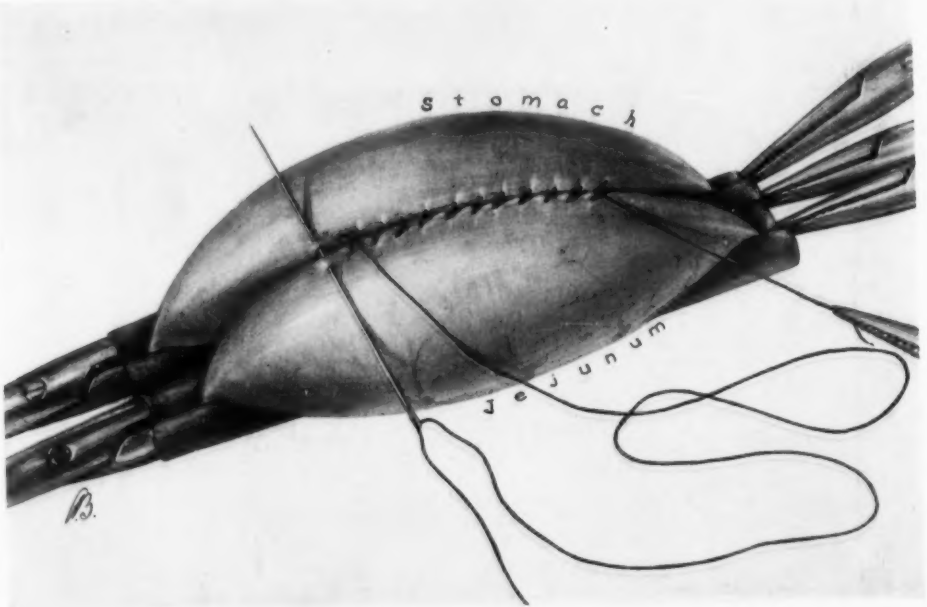


FIG. III. The first portion of the jejunum and the posterior surface of the stomach, after the application of rubber-shod clamps, are approximated, and the first stitch of the posterior row is taken, a continuous stitch of medium silk. It is of the greatest importance to include the submucosa in the stitch. (Care is taken not to disturb the direction of the first portion of the jejunum at the duodeno-jejunal angle, but to approximate it to the posterior surface of the stomach according to the way the jejunum lies in each individual case, whether it be downward and to the left, or downward and to the right.)

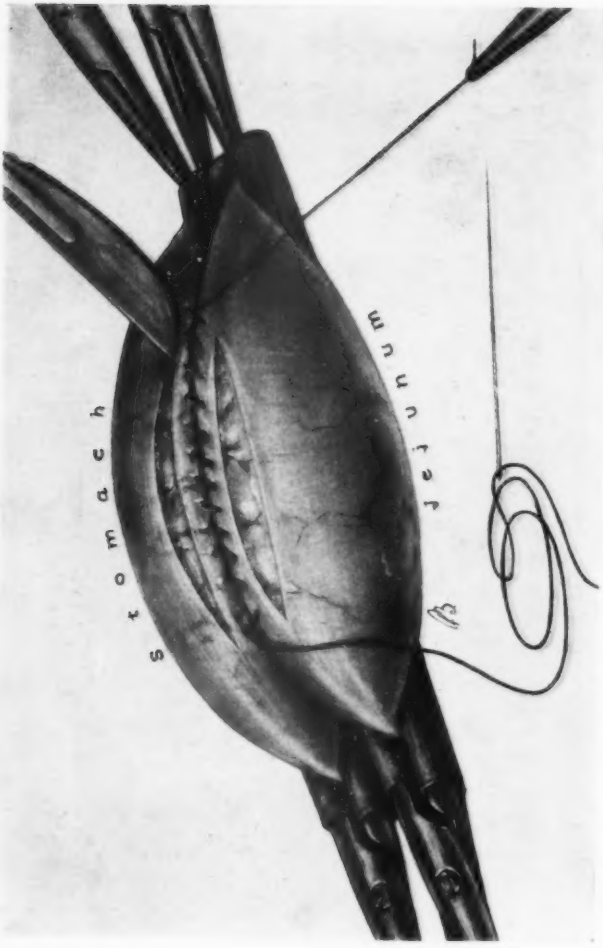


FIG. IV. Incisions are made down to, but not including, the mucosa, in the stomach and duodenum.

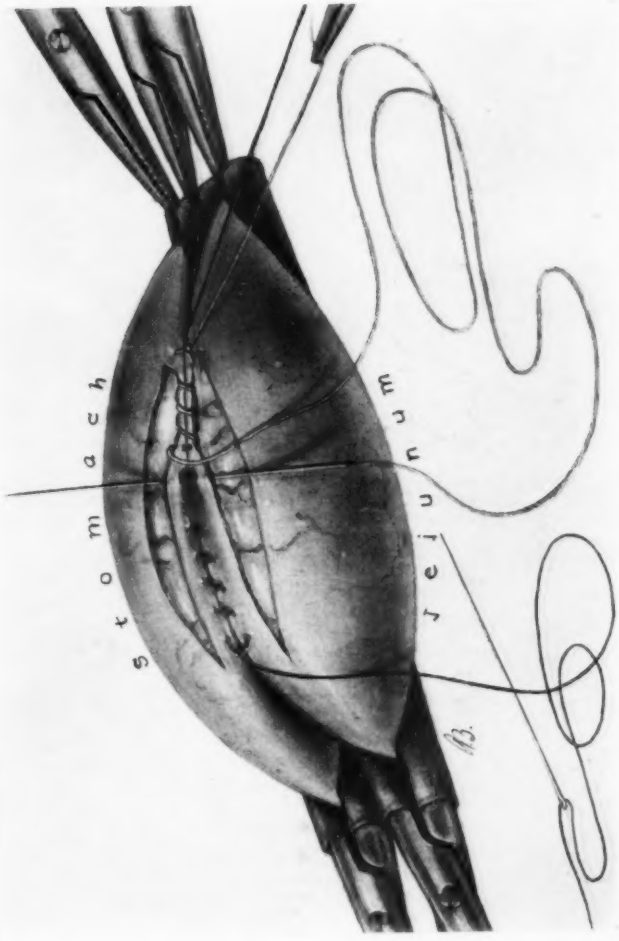


FIG. V. The second stitch of the posterior row is now taken. This is of No. 2 plain catgut and includes the serosal, muscular and submucosal coats.

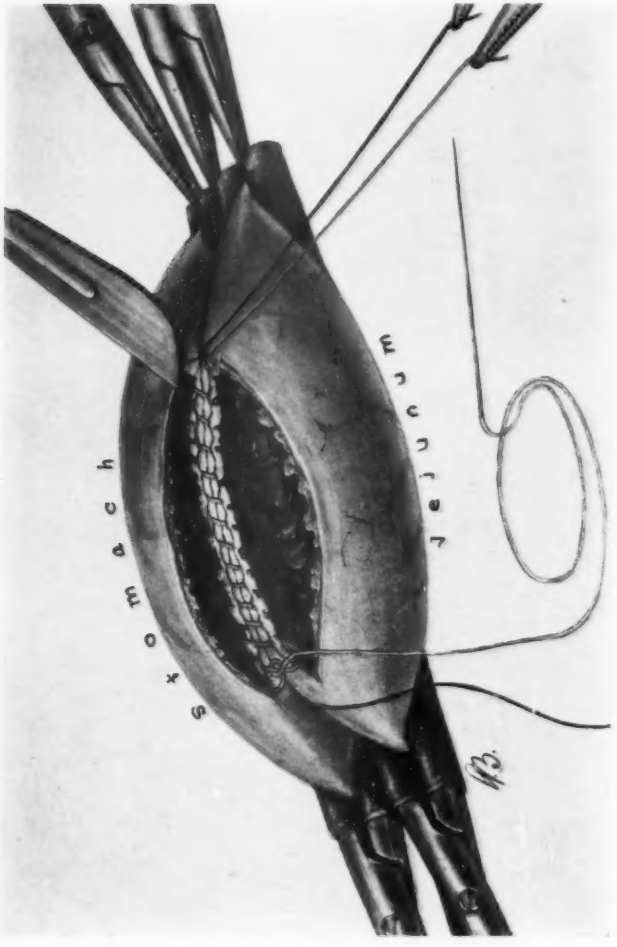


FIG. VI. Incisions are made through the mucosa into the lumen of the stomach and jejunum

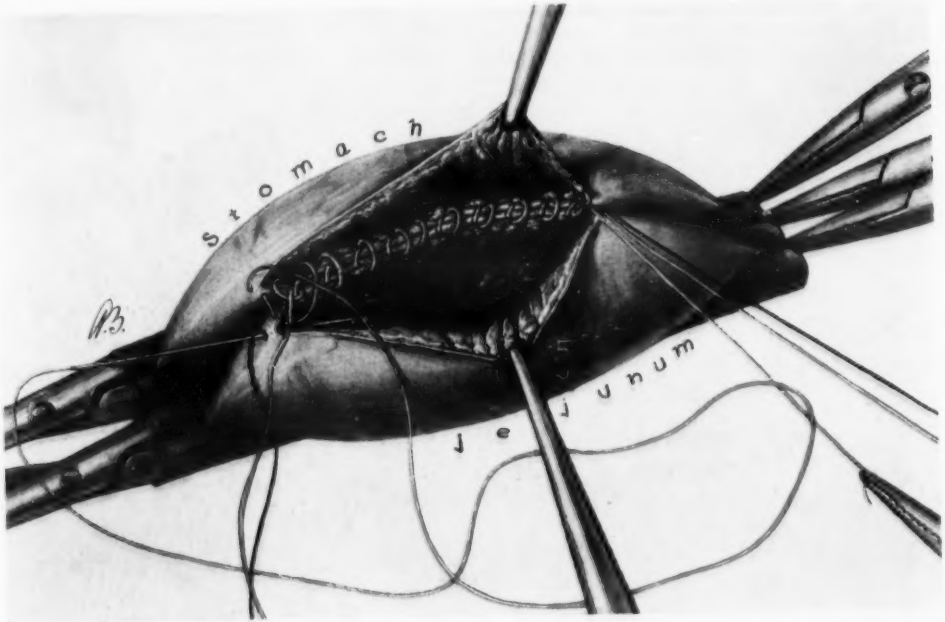


FIG. VII. The third stitch of the posterior row is taken; it is of No. 2 plain catgut and approximates the cut mucosal edges of the stomach and the jejunum. The point of the needle is seen turning at the far angle of the anastomosis to start back to approximate the mucosa of the anterior row of the anastomosis.

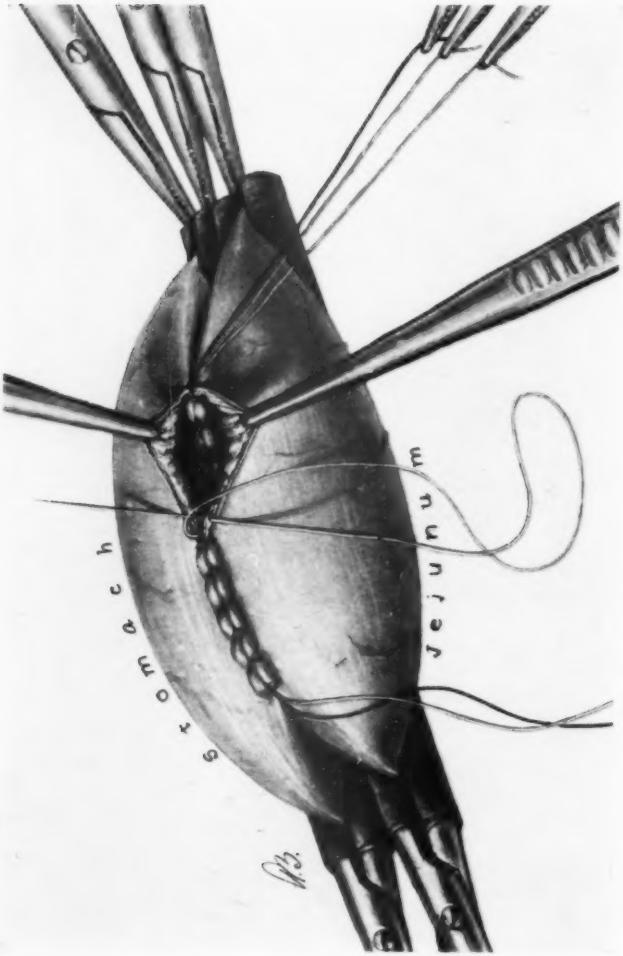


FIG. VIII. As soon as this first stitch of the anterior row is complete, it will be tied to its starting end, held by the lower clamp seen in this illustration.

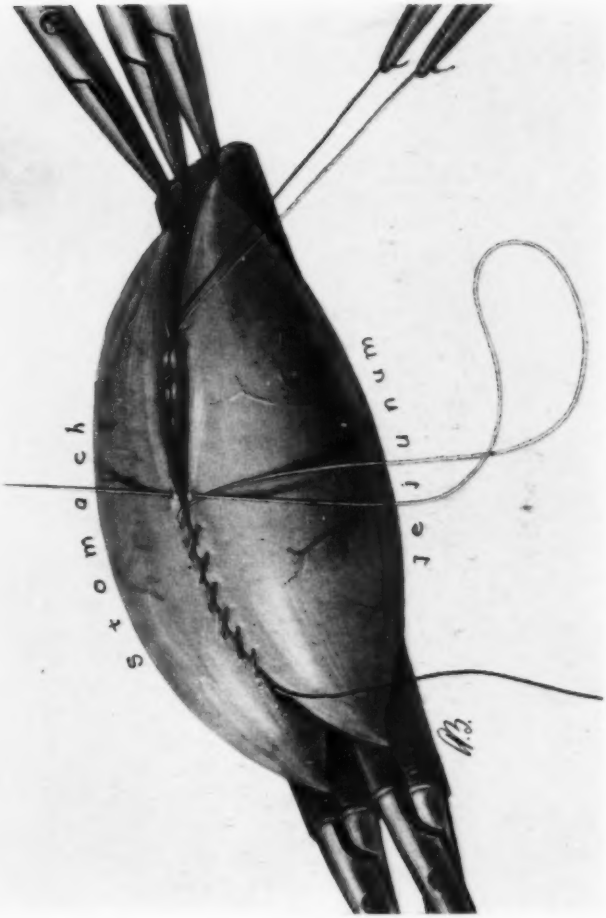


FIG. IX. The second stitch is continued around in similar fashion to form the second stitch of the anterior row of the anastomosis.

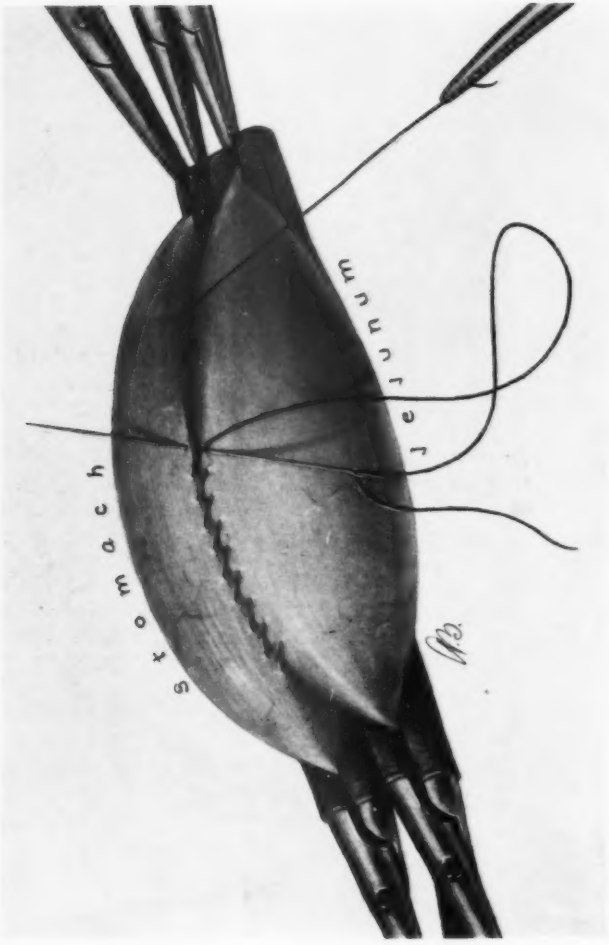


FIG. X. The first stitch of silk is likewise completed. (The clamps are removed before this stitch is taken.)

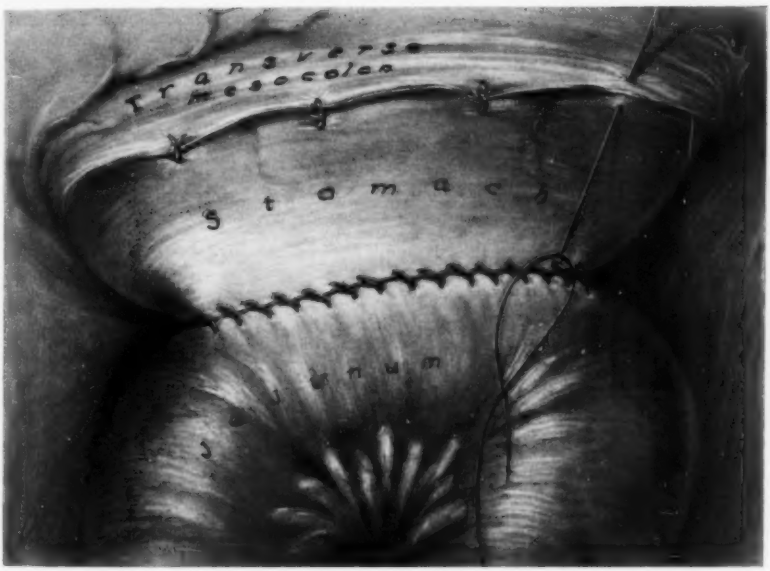


FIG. XI. Interrupted stitches of catgut are taken to fix the transverse mesocolon to the stomach well back from the anterior row of the anastomosis.

BOOK REVIEWS

(These reviews represent the individual opinions of the reviewers and not necessarily those of the members of the Editorial Board of this Journal.)

The Diagnosis and Treatment of Diseases of the Peripheral Arteries. By SAUL S. SAMUELS, A.M., M.D., Oxford Medical Publications. 260 pp. illus. $3.50. (*Oxford University Press, New York, 1936.*)

Very superficial and by no means a comprehensive work, this little book, more than anything else, is a summary of the author's views on thrombo-angiitis obliterans and its treatment by intravenous salt solution, as exemplified in his various publications.

As such it is good, but when a man essays to write a book on the diagnosis and treatment of peripheral vascular diseases and practically omits every vestige of the very latest thought on the subject, he cannot complain if his scientific interest is seriously questioned. One may feel that ganglionectomy is not a sound procedure, that the various studies concerning the sympathetic nervous system are unimportant, and that the Pavaex treatment has not justified itself, yet men of broad training and deep understanding have literally flooded the literature with their studies on these subjects. Dr. Samuels does himself little credit in ignoring them. The Pavaex treatment, for example, is given exactly one brief paragraph.

Further comment on the book is, perhaps, unnecessary.

B. M. B.

Clinical Miscellany. Volume II: 1935. The Mary Imogene Bassett Hospital, Cooperstown, N. Y. 218 pp. $3.00. (*Charles C. Thomas, Publisher. Springfield, Ill., 1935.*)

This little volume, the second in a series which was started in 1934, records a variety of clinical studies conducted by the staff of the Mary Imogene Bassett Hospital of Cooperstown, New York. It contains twenty separate papers which are, for the most part, based upon case studies of patients exhibiting unusual diseases or unusual manifestations of common diseases. The reports are in no sense comprehensive reviews and they are not burdened by large bibliographies. On the other hand, they set forth clinical studies which have been carried out with exemplary thoroughness. The brief and frequently stimulating discussion of each problem contains references to the more recent relevant literature.

J. B., III

Names of Surgical Operations. Compiled and arranged by the Western Surgical Association. Edited by C. E. Black. (*Bruce Publishing Co., St. Paul, Minn., 1935.*)

The multiplicity of descriptive names of surgical operations prompted the preparation of the present compilation. All types of surgical operations are listed

according to the organs or regions of the body involved. The book should prove useful in bringing about a uniform system of surgical nomenclature.

A. G.

Manual of Clinical Laboratory Methods. By PAULINE S. DIMMITT, Ph.G., 156 pp. with 36 engravings including 7 full page colored plates. (*F. A. Davis Co., Philadelphia, 1934.*)

A concise summary of the methods in common use in clinical laboratory procedures, designed for the use of students and internists. Besides the usual methods for the examination of urine, blood, sputum, etc., the methods of blood transfusion tests, Wassermann tests and the hormone test for pregnancy are included. The book is succinctly and well written.

A. G.

John Whitridge Williams. Academic Aspects and Bibliography. By J. MORRIS SLEMONS. 109 pp. $1.50. (*The Johns Hopkins Press, Baltimore, 1935.*)

This attractive little volume sketches the academic career and achievements of the late John Whitridge Williams. The author is well equipped for his task, for not only was he closely associated with Dr. Williams during those stirring years when prenatal care, the textbook, pubiotomy and funnel pelvis followed each other in quick succession, but he was also one of those who went forth to high posts in this country to spread the teachings of his Chief. At the close of the nineteenth century, American obstetrics was a backward, scarcely respectable branch of medicine over which the midwife's shadow lay heavily. Graphically and with evident devotion, Dr. Slemons tells of the important part that Dr. Williams played in raising obstetrics from a mere handicraft to a dignified scientific branch of medicine. Of particular value is the complete bibliography of Dr. Williams' publications, prepared by Miss Louise D. Coulter-King, Assistant Librarian, Medical and Chirurgical Faculty of Maryland, and Miss Louise M. Diggs, for many years Dr. Williams' secretary.

By limiting the scope of his study to academic aspects, Dr. Slemons has had to reduce to a minimum personal reminiscences, and to omit altogether those little traits and foibles of character which help so much in creating a living portrait. It is true that in certain sections of the book, particularly in the quotation from Dr. Williams' letter to his Resident, one feels undoubtedly the presence of a great personality. But these touches are all too few, and in the book as a whole the man does not appear. It is to be hoped that Dr. Slemons, or someone with an equally facile pen, will undertake a full-length biography of Dr. Williams in which this great pioneer in the science of obstetrics in America will really live and move and have his being.

N. J. E.

The Cerebrospinal Fluid and Its Relation to the Blood. By SOLOMON KATZENELBOGEN. 468 pp. $5.00. (*Johns Hopkins Press, Baltimore, 1935.*)

It has been the purpose of the author to gather together and to assay critically literature dealing with physiological, biochemical and clinical problems presented by the cerebrospinal fluid.

The first portion of the book has to do with the physiology and biochemistry of the fluid. In his treatment of these problems, the author has assembled very numerous data many of which would appear to make a minor contribution to the questions involved and so confuse the issues and detract from the interest of the discussion. The discussion of the chemical nature of the fluid is frankly admitted by the author to cause him theoretical difficulties. These difficulties he has been unable to overcome nor has he been able to establish any rigid criterion for deciding whether the fluid is an ultrafiltrate or a secretion. He consequently makes no contribution to this subject except by his presentation of the data and of the views which have sprung up around it. This, indeed, appears to be the real virtue of the first portion of the book: it considers the literature exhaustively and presents a considerable portion of the critique which has developed with the subject.

The second and larger portion of the book should prove of real aid to the clinician. It has a wide scope and deals comprehensively with the changes in concentration of the electrolytes and non-electrolytes of the fluid and their diagnostic value, and with the barrier between blood and cerebrospinal fluid together with the methods of testing and altering its permeability. There is a chapter on arsenotherapy and one on bismuth therapy.

Dr. Katzenelbogen has given us an excellent book for reference on the cerebrospinal fluid,—the most complete we have in English. Close study of the material which he presents should, as he hopes, provoke stimulation for further investigations in a field in which so many important points are far from settled.

L. B. F.

Alcohol and Anaesthesia. By W. BURRIDGE. 65 pp. 2/6. (*Williams and Norgate, London, 1934.*)

According to the preface this small volume attempts to give an explanation of some of the neural and psychic effects associated with the drinking of alcoholic beverages. The author attempts an explanation on the basis of the idea that central neurons possess "two sources of energy and inherent rhythmicity," but rambles somewhat in expounding his unconventional theories so that it is doubtful whether his treatise will serve to aid in any way the solution of the alcohol problem.

E. K. M., JR.

Prescription Writing and Formulary. By CHARLES SOLOMON. 351 pp. 32 illus. $4.00. (*J. B. Lippincott Co., Philadelphia, 1935.*)

This is essentially a book on prescription writing and should be useful to students and young practitioners of medicine. Part I consists of an introduction

which gives a brief historical sketch of prescription writing and a discussion of such subjects as the absorption and excretion of drugs, channels of administration, and selection and care of syringes and needles. In Part II the essential elements of prescription writing are discussed, and it is interesting to note that the author very strongly favors the use of Latin. In Part III a rather extensive formulary is given, the drugs being arranged according to their therapeutic use. Here numerous typical prescriptions are set forth by the author, who states that these are meant not to be memorized but to serve the purpose of pointing out the simplicity of rational prescribing.

E. K. M., Jr.

Child Psychiatry. By Leo Kanner, Associate Professor of Psychiatry at the Johns Hopkins University. 1935. 527 pp. $6.00. (*Charles C. Thomas, Springfield, Illinois and Baltimore, Maryland.*)

Dr. Kanner has given us the first textbook on child psychiatry written in the English language. He has approached his problem from the standpoint of the psychobiologist and in his book presents the results of his own experience in his daily work with the children of the Harriet Lane Pediatric Hospital. As a result of this extensive clinical experience, the book is filled with telling case material studied in a manner compatible with the best of trained common sense. The child in health or in disease is viewed as a unified organism reacting to the forces within himself and to the forces of his environment. It is this concept of the child as a reactive organism which has allowed Dr. Kanner to bring into play all the sciences which contribute in any way to the understanding of the reaction.

Chapter 1 outlines the various schools of approach to the problems of mind and behavior, and chapter 2 tells us how the author has tried to avoid too much stress upon any special theories or schools and has endeavored to maintain a pluralistic attitude, that is, one in which there is a determination to see all the factors at work, to see how they work, the setting in which they occur, and the opportunities offered the physician for bringing about the desirable modifications.

The second section outlines the procedure of examination and stresses the focusing on the complaint factor. Succeeding chapters deal with the factors of age, intelligence, somatic status, etc. Part II deals with difficulties resulting as sequels to physical illness; personality difficulties expressing themselves in the form of involuntary partial dysfunctions; and the personality difficulties representing total dysfunctions of the individual.

Dr. Kanner has performed a notable service in giving us a book replete with facts and careful case histories. He has admirably accomplished his purpose, which was to write a textbook that would serve not only the general medical man and the pediatrician, but one that would be helpful to the specialist trained in the management of behavior throughout the childhood period. Extensive references to the literature are included.

Dr. Kanner presents his material in a broad, objective, unbiased, and practical

way. The book is one that every psychiatrist will want to own, and that all other medical men ought to own.

T. A. B. K.

Über Carcinoma, Sarcome und Lymphomatosis infiltrans bei weissen Mäusen. By JOHS. V. ANDERSEN. 143 pp., unbound. Illustrated. (*Levin & Munksgaard, Kopenhagen, 1934.*)

This is a monograph which emphasizes the work of the author in attempting to prove or disprove the claim of Prof. Heidenhain (1928–30) that an autolysate of cancer cells, containing products liberated by lysis of cancer cells, can produce tumors when injected into mice. Some of the work deals with the attempts to produce tumors in mice by using materials from human tumors. Inasmuch as the average incidence of spontaneous tumors in mixed strains of mice is approximately 7 per cent and this figure is about as great as in the author's experimental series (7.3% of 560 mice) or in the control series (5.5% of 560 animals), he is inclined to make this statement, "The writer feels justified in looking upon his own tumors as spontaneous tumors and in assuming that the tumors found by Heidenhain were also spontaneous tumors." Evidence is presented that tissue autolysate might influence the reaction of the lymphatic and hematopoietic apparatus in a definite direction. The author also discusses his findings in the condition known as lymphomatosis infiltrans. The book also includes a good review of early work on attempts to produce tumors in animals with materials (tumor cells, extracts, etc.) derived from human tumors.

G. O. G.

Nursing Mental Diseases. By HARRIET BAILEY. 3rd ed. Revised. 258 pp. $2.50. (*The MacMillan Co., New York, 1935.*)

There is so much confusion of thought in the present flood of literature on Psychiatry, and in its multitudinous branches, and so intricate and technical in its exposition, that the nursing profession welcomes with much gratification Miss Harriet Bailey's revised "Nursing Mental Diseases."

Miss Bailey has covered this particular field of nursing with thoroughness and has dealt with the subject from a very helpful point of view for the nurse. She has fully acquainted herself with the latest methods and theories, and has handled this complex study with the utmost simplicity and clarity. We are grateful to her for presenting material which is within the realm of the nurses' needs and without delving into the mysteries and debatable concepts of her subject. We regret, however, that we do not find specific instructions on how to handle actual types of behavior disturbances, but perhaps the author feels that this management is too spontaneous a reaction to be treated in a textbook.

In this third revision, the author has succeeded in producing a book that is a combination of comprehensiveness and practicability and is undoubtedly a book of great usefulness to students interested in the fundamentals of Psychiatric Nursing. It should be included in libraries of all Training Schools for Nurses.

B. A. M.

Bacteriology for Nurses. By M. A. SMEETON, M.A. Fourth edition revised. 352 pp. Illus. $3.00. (*The Macmillan Company, New York, 1935.*)

A revised edition of a valuable and much used text for nurses bringing it up to date in subject matter and the use of the new nomenclature suggested by the Committee of the Society of American Bacteriologists. There have been some changes in organization of material, but the content still deals mainly with the study of pathogenic microorganisms—the branch which is of greatest use to the student of nursing.

L. S. K.

Tuberculosis. By GERALD B. WEBB. 205 pp. Illus. $2.00. (*Clio Medica.*) (*Paul B. Hoeber, Inc., New York, 1936.*)

This small volume outlines, in a well-arranged and authoritative form, the high points in the development of our knowledge of Tuberculosis from ancient times to the present. It is one of a series of books presenting, in a unified way, the historical side of special subjects, thereby providing instructive reading for the average doctor and valuable reference books for students of the subject. Doctor Webb has divided his book into chapters which deal with the evolution of the most important phases of Tuberculosis, and we are shown the age-old struggle of facts with theories in the realms of pathology, contagion, diagnosis, treatment, and the rest.

The chapter dealing with contagion is of especial interest, in that it shows the slow progress of this theory, whose truth seems so obvious to us today, from the early suspicions of Aristotle to the final proofs furnished by Villemin and by Koch. In the field of pathology, we are impressed with the importance of the fundamental observations of Sylvius, Morton, Baillie, Stark and others, which are followed by the clear descriptions of such men as Bayle, Laennec and Louis, who recognized the unity of the different types of Tuberculosis and pointed the way that modern thought was to follow. The slow development of rational treatment, and some of the almost unbelievable ancient methods—a few of which survived to comparatively recent times—are described in an entertaining manner.

On the whole, this book is well compiled and instructive and can be highly recommended to all those who wish to acquire the broader background for a knowledge of Tuberculosis which is achieved through the historical approach.

A. M. F.

Allergy of the Nose and Paranasal Sinuses. By FRENCH K. HANSEL. 820 pp. $10.00. (*C. V. Mosby Co., St. Louis, 1936.*)

This "monograph on the subject of allergy as related to otolaryngology" presents a most comprehensive review of the literature with a very complete bibliography. In fact, so many reports are included that one is likely to become confused, had not the author given us the gist of the subject in a brief discussion at the end of each chapter. The sections on the physiology, biochemistry and bacteriology of the nose and paranasal sinuses are excellent. The chapter dealing

with allergic lesions of the ear places too much emphasis upon allergy as the cause of Ménière's symptom-complex.

A large part of the text is very technical and is of interest chiefly to the specialist in allergy. The illustrations are very good and very few typographical errors are noted. On the whole, this is a valuable reference book, even though one may not entirely agree with all of the conclusions.

J. W. B.

Synopsis of Clinical Laboratory Methods. By W. E. BRAY. 324 pp. Illus. $3.75. (*C. V. Mosby Co., St. Louis, 1936.*)

This compact little volume is truly a synopsis of methods, not only for urinalysis, blood and stool examination, but also for many other procedures, including the chemical examination of blood, bacteriology, serology and even surgical pathology. The book is well organized. A great deal of useful information will be found to be easily accessible. As a whole it is up to date, although such modern procedures as the fractional intravenous phenolsulphonephthalein test and hematocrit technique are not adequately discussed. On the other hand, whereas the newer differential methods are mentioned, there is no explanation of the manner in which the various types of leucocytes may be distinguished. There are a number of useful illustrations but many of the color plates could be improved. The usefulness of this handbook would be further increased if pitfalls in technique, and the way in which they can be overcome, were dealt with.

M. M. W.

Lobar Pneumonia and Serum Therapy. By FREDERICK T. LORD and RODERICK HEFFRON. 91 pp. $1.00. (*The Commonwealth Fund, New York, 1936.*)

This brief treatise on the methods of serum treatment of lobar pneumonia is based largely on the results of an experiment on the use of concentrated serum by the general practitioner in the decentralized sections of Massachusetts. The significant topics include methods of clinical diagnosis, selection of cases for serum treatment, the determination of types of pneumococcus, the technic of administration of the serum including the correct dosage as judged from the authors' experience, and also precautions to be observed to control possible untoward reactions due either to the patient's sensitivity to serum protein or to the concentrated serum itself. The method outlined is satisfactory as a guide in the use of serum therapy for lobar pneumonia. By application of the writers' technic the mortality rate of Type I lobar pneumonia decreased from 25% to 11% and of Type II from 41% to 27%. These results compare favorably with those previously obtained in large urban hospitals, and indicate the practicability of the use of concentrated antipneumococcus serum by the general practitioner. For the most part the procedure advised has been shown by earlier investigators to be good practice, and in reality the present work supplies a confirmation or summary of many clinical studies.

L. D. F.

Manual of Diabetes. By J. J. CONYBEARE. 123 pp. $2.00. (*Oxford University Press, London, 1935.*)

The author gives us the fundamentals of diabetic diagnosis and treatment concisely and clearly. According to his preface, the book is designed both for physicians and the laity, although the discussion would appear to be hardly simple enough for the average layman. It would be quite useful, however, for the practitioner, interne, and medical student.

There are certain precepts in the book which, in our opinion, would hardly be applicable to the case of every diabetic patient. For example, there is no warning given against the use of adrenalin for hypoglycemic shock in elderly patients. In some cases spinal anesthesia or ethylene is to be preferred to gas and oxygen; and it would seem questionable whether an ounce of castor oil should be introduced by stomach tube into all coma patients. Moreover, insufficient stress is laid upon fluid and electrolyte replacement.

Nevertheless, the book is very well written, and if the practitioner follows its guidance closely, grave errors in treatment will very rarely be made.

J. E. H.

Personal and Community Health. By CLAIR ELSMERE TURNER, M.A., Dr.P.H. 4th Edit., 680 pp. Illus. $3.00. (*C. V. Mosby Co., St. Louis, 1935.*)

The author presents the fourth edition of his textbook for the use of college students. Part I, devoted to the whole general field of personal hygiene, consists of twenty chapters, covering all of the body functions and including chapters on nutrition, heredity, and body mechanics. Part II contains twelve chapters on community health, and deals with the development of preventive medicine, problems connected with communicable diseases, food control, water supply, maternal, school, industrial hygiene, and public health administration. There is a valuable appendix dealing especially with the contagious diseases and summarizing for each disease the points for its recognition, the etiological agent, the mode of transmission, the incubation period, the period of communicability, and the methods of control.

There are few things in the text that call for adverse criticism. Anatomical and physiological explanations are simply and yet on the whole accurately given of the ground covered in the part devoted to personal hygiene. The author is not a doctor of medicine and occasionally his simplified discussions of disease are less accurate than what he has to say of normal function. The section on community health is well done and gives evidence of Dr. Turner's long experience as a sanitarian. The illustrations are good and the text is well written. A glossary and an index are appended.

While a general textbook covering such a wide field is bound to leave much to be desired, when consulted by specialists, this volume seems to the reviewer to accomplish what the author intended it to do—to present a reasonably accurate, up-to-date, and yet simple text for college students who are surveying the whole field of hygiene in a single course.

M. B.

The Parathyroids in Health and Disease. By DAVID H. SHELLING. 335 pp., illust. $6.00. (*C. V. Mosby Co., St. Louis, 1935.*)

The book deals especially with the quantitative relations of calcium and phosphates in the body, insofar as they are controlled by the parathyroids. These chemical relations are carefully considered and efforts are made to explain the still obscure mechanism of the actual loss of calcium. Emphasis is laid upon the accurate balance required for normal conditions and the consequent necessity for normal activity of the parathyroids, since either excess or deficiency of their hormone leads to grave disturbances.

While certain other abnormalities such as the alkalosis from hyperventilation can disturb this balance, it becomes evident, from comparison of the action of the parathyroids with that of Vitamin D, that these are quite distinct processes. This comparison is especially illuminating and the description of the contrasting effects upon the bones is well worked out.

The book is evidently the result of long and thoughtful study of the whole subject, and although there is much repetition—which is true also of the literature references—it would seem to be the best discussion of the parathyroids which has yet appeared and is also commendable in that it points out the many obscurities which remain for further investigations.

M.

Obstetrics for the General Practitioner. By J. P. GREENHILL. Ed. by MORRIS FISHBEIN. 304 pp., illus. $3.00. (*National Medical Book Company, New York, 1935.*)

This rather brief volume adds one more to the rapidly growing collection of treatises on Obstetrics which have appeared in the last five years. As the author intimates, it might well be termed a condensation of DeLee's well known textbook. To many, it will suffer from being too dogmatic about various highly debatable questions, as witness the statement, "the low cervical cesarean section is far safer than the classic operation." Furthermore, the comparative space allotted to various subjects is to be regretted, particularly in a book intended for the general practitioner, for whereas twenty-six pages are consumed in a discussion of the rare diseases of the membranes, only sixteen are given to the important topic of puerperal infection. In general, however, it preaches strict conservatism and hence becomes a valuable work for the rank and file of the medical profession.

C. H. P.

Food and Beverage Analyses. By MILTON A. BRIDGES. 246 pp. $3.50. (*Lea and Febiger, Washington Square, Philadelphia, 1935.*)

The main part of the book is devoted to a table of the nutritive and caloric values of foods, classified in a helpful manner. Each food is considered quantitatively by portions, recorded in a household measure together with its metric equivalent. The protein, carbohydrate and fat content of such a portion of each food is given in both absolute amount and percentage; the caloric content

of each portion is likewise denoted. Brief consideration of the caloric requirements of individuals engaged in various activities, together with a table of heights and weights, provides the reader with additional data that might be needed in utilizing the tables.

The book is thoroughly modern and is so much more complete than many of its predecessors that it may well lay claim of justifying the author's avowed intention of filling "an hiatus in the armamentarium of all those interested in nutrition." Two departures from the conventional formula of a book of this type deserve recognition: first, fruits and vegetables have been analyzed in the form in which they are eaten; secondly, recognizing the increasing use of canned and packaged foods the author has ignored the hitherto inviolable practice of recording only fresh and non-commercial products and has seemingly built his table around the staple items of the American diet, the processed foods. By intensive search of the literature, by original analyses and by data furnished on commercial products by manufacturers, the author has overlooked very few foods. Even strained foods, so much in vogue in pediatrics, are detailed according to the various manufacturers.

The early chapters of the book discuss proteins, carbohydrates, fats and water, and outline their utilization and the bodily requirements, together with selected examples of foods rich and poor in each. The concluding chapters perform essentially the same service on mineral constituents and vitamins.

For the dietitian and nurse faced with constant calculation of calories from the necessity of introducing pleasant variety in menus this book would be of considerable aid. For the clinician who desires a source book on the composition and caloric value of different foods or who would arrange his own menus for his patients, this book deserves recommendation.

H. D. K.

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